

Patent
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NEW APPLICATION TRANSMITTAL
UTILITY

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Transmitted herewith for filing is a **utility** patent application:

Inventor(s): Jerry Pelletier, Philippe Gros, Michael DuBow

Title: DNA SEQUENCES FROM *STAPHYLOCOCCUS AUREUS*
BACTERIOPHAGE 77 THAT ENCODE ANTI-MICROBIAL
POLYPEPTIDES

I. PAPERS ENCLOSED HEREWITH FOR FILING:

51 Page(s) of Specification 109 Pages of Tables
4 Page(s) Claims
1 Page(s) Abstract
13 Sheets of Drawings Informal ✓ Formal

II. ADDITIONAL PAPERS ENCLOSED IN CONNECTION WITH THIS FILING:

- ☐ Power of Attorney.
☐ Declaration.
☐ Assignment to _____ and assignment cover sheet.

SD-105779.1

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(37 C.F.R. §1.10)

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- ☐ Verified Statement establishing "Small Entity" under 37 CFR §§ 1.9 and 1.27.
- ☐ Priority Document No(s): _____.
- ☐ Information Disclosure Statement w/PTO 1449 ☐ References
- ☐ Preliminary Amendment.

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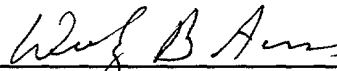
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Respectfully submitted,

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Dated: September 28, 1999

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**APPLICATION
FOR
U.S. LETTERS PATENT**

**DNA SEQUENCES FROM *STAPHYLOCOCCUS AUREUS*
BACTERIOPHAGE 77 THAT ENCODE ANTI-MICROBIAL
POLYPEPTIDES**

BY: Jerry Pelletier, Philippe Gros, Michael DuBow

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DESCRIPTION

DNA SEQUENCES FROM *STAPHYLOCOCCUS AUREUS* BACTERIOPHAGE 77 THAT ENCODE ANTI-MICROBIAL POLYPEPTIDES

5

RELATED APPLICATIONS

10 This application claims the benefit of United States Provisional Application
No. 60/110,992, filed December 3, 1998, which is hereby incorporated by reference
in its entirety, including drawings.

BACKGROUND OF THE INVENTION

15 This invention relates to the identification of antimicrobial agents and of
microbial targets of such agents, and in particular to the isolation of bacteriophage
DNA sequences, and their translated protein products, showing anti-microbial
activity. The DNA sequences can be expressed in expression vectors. These
expression constructs and the proteins produced therefrom can be used for a variety
20 of purposes including therapeutic methods and identification of microbial targets.

The following description is provided to assist the understanding of the
reader. None of the information provided or references cited is admitted to be prior
art to the present invention.

25 The frequency and spectrum of antibiotic-resistant infections have, in recent
years, increased in both the hospital and community. Certain infections have
become essentially untreatable and are growing to epidemic proportions in the
developing world as well as in institutional settings in the developed world. The
staggering spread of antibiotic resistance in pathogenic bacteria has been attributed
to microbial genetic characteristics, widespread use of antibiotic drugs and changes
30 in society that enhance the transmission of drug-resistant organisms (for a review,
see Cohen, 1992). This spread of drug resistant microbes is leading to ever-
increasing morbidity, mortality and health-care costs.

There are over 160 antibiotics currently available for treatment of microbial
infections, all based on a few basic chemical structures and targeting a small number

of metabolic pathways: bacterial cell wall synthesis, protein synthesis, and DNA replication. Despite all these antibiotics, a person could succumb to an infection as a result of a resistant bacterial infection. Resistance now reaches all classes of antibiotics currently in use, including: β -lactams, fluoroquinolones, aminoglycosides, macrolide peptides, chloramphenicol, tetracyclines, rifampicin, folate inhibitors, glycopeptides, and mupirocin. There is thus a need for new antibiotics, and this need will not subside given the ability bacteria have to overcome each new agent synthesized. It is also likely that targeting new pathways will play an important role in discovery of these new antibiotics. In fact, a number of crucial cellular pathways, such as secretion, cell division, and many metabolic functions, remain untargeted today.

Most major pharmaceutical companies have on-going drug discovery programs for novel anti-microbials. These are based on screens for small molecule inhibitors (e.g., natural products, bacterial culture media, libraries of small molecules, combinatorial chemistry) of crucial metabolic pathways of the micro-organism of interest. The screening process is largely for cytotoxic compounds and in most cases is not based on a known mechanism of action of the compounds. Classical drug screening programs are being exhausted and many of these pharmaceutical companies are looking towards rational drug design programs. Several small to mid-size biotechnology companies, as well as large pharmaceutical companies, have developed systematic high-throughput sequencing programs to decipher the genetic code of specific micro-organisms of interest. The goal is to identify, through sequencing, unique biochemical pathways or intermediates that are unique to the microorganism. Knowledge of the function of these bacterial genes, may form the rationale for a drug discovery program based on the mechanism of action of the identified enzymes/proteins. However, one of the most critical steps in this approach is the ascertainment that the identified proteins and biochemical pathways are 1) non-redundant and essential for bacterial survival, and 2) constitute suitable and accessible targets for drug discovery. These two issues are not easily addressed since to date, 18 prokaryotic genomes have been sequenced and 200 sequenced genomes are expected by the year 2000. For a majority of the sequenced genomes, less than 50% of the open reading frames (ORFs) have been linked to a known function. Even with the genome of *Escherichia coli* (*E. coli*), the most extensively studied bacterium, less than two-thirds of the annotated protein coding

genes showed significant similarity to genes with ascribed functions (Rusterholtz and Pohlschroder, 1999). Thus considerable work must be undertaken to identify appropriate bacterial targets for drug screening.

5

SUMMARY OF THE INVENTION

The present invention is based on the identification of, and demonstration that, specific DNA sequences of a bacteriophage, when introduced into a host bacterium can kill, or inhibit growth, of the host. Thus, these DNA sequences are anti-
10 microbial agents. Information based on these DNA sequences can be utilized to develop peptide mimetics that can also function also as anti-microbials. The identification of the host bacterial proteins, targeted by the anti-microbial bacteriophage DNA sequences, can provide novel targets for drug design and compound screening.

15 In this regard, the terms "inhibit", "inhibition", "inhibitory", and "inhibitor" all refer to a function of reducing a biological activity or function. Such reduction in activity or function can, for example, be in connection with a cellular component (e.g., an enzyme), or in connection with a cellular process (e.g., synthesis of a particular protein), or in connection with an overall process of a cell (e.g., cell
20 growth). In reference to cell growth, the inhibitory effects may be bactericidal (killing of bacterial cells) or bacteriostatic (i.e., stopping or at least slowing bacterial cell growth). The latter slows or prevents cell growth such that fewer cells of the strain are produced relative to uninhibited cells over a given time period. From a molecular standpoint, such inhibition may equate with a reduction in the level of, or
25 elimination of, the transcription and/or translation of a specific bacterial target(s), or reduction or elimination of activity of a particular target biomolecule.

In a first aspect the invention provides methods for identifying a target for antibacterial agents by identifying the bacterial target(s) of at least one inhibitory gene product, e.g., protein from ORFs 17, 19, 43, 102, 104, and 182 of
30 bacteriophage 77 or a homologous product. Such identification allows the development of antibacterial agents active on such targets. Preferred embodiments for identifying such targets involve the identification of binding of target and phage ORF products to one another. The target molecule may be a bacterial protein or other bacterial biomolecule, e.g., a nucleotprotein, a nucleic acid, a lipid or lipid-

containing molecule, a nucleoside or nucleoside derivative, a polysaccharide or polysaccharide-containing molecule, or a peptidoglycan. The phage ORF products may be subportions of a larger ORF product that also binds the host target. Exemplary approaches are described below in the Detailed Description.

5 Additionally, the invention provides methods for identifying targets for antibacterial agents by identifying homologs of a *Staphylococcus aureus* target of a bacteriophage ORFs 17, 19, 43, 102, 104, or 182 product. Such homologs may be utilized in the various aspects and embodiments described herein.

10 The term “fragment” refers to a portion of a larger molecule or assembly. For proteins, the term “fragment” refers to a molecule which includes at least 5 contiguous amino acids from the reference polypeptide or protein, preferably at least 6, 8, 10, 12, 15, 20, 30, 50 or more contiguous amino acids. In connection with oligo- or polynucleotides, the term “fragment” refers to a molecule which includes at least 15 contiguous nucleotides from a reference polynucleotide, preferably at least 18, 21, 24, 30, 36, 45, 60, 90, 150, or more contiguous nucleotides. Also in preferred embodiments, the fragment has a length in a range with the minimum as described above and a maximum which is no more than 90 % of the length (or contains that percent of the contiguous amino acids or nucleotides) of the larger molecule (e.g., of the specified ORF), in other embodiments, the upper limit is no more than 60, 70, or 80% of the length of the larger molecule.

20 Stating that an agent or compound is “active on” a particular cellular target, such as the product of a particular gene, means that the target is an important part of a cellular pathway which includes that target and that the agent acts on that pathway. Thus, in some cases the agent may act on a component upstream or downstream of the stated target, including a regulator of that pathway or a component of that pathway. In general, an antibacterial agent is active on an essential cellular function, often on a product of an essential gene.

25 By “essential”, in connection with a gene or gene product, is meant that the host cannot survive without, or is significantly growth compromised, in the absence or depletion of functional product. An “essential gene” is thus one that encodes a product that is beneficial, or preferably necessary, for cellular growth *in vitro* in a medium appropriate for growth of a strain having a wild-type allele corresponding to the particular gene in question. Therefore, if an essential gene is inactivated or inhibited, that cell will grow significantly more slowly or even not at all. Preferably

growth of a strain in which such a gene has been inactivated will be less than 20%, more preferably less than 10%, most preferably less than 5% of the growth rate of the wild-type, or not at all, in the growth medium. Preferably, in the absence of activity provided by a product of the gene, the cell will not grow at all or will be non-viable, at least under culture conditions similar to normal *in vivo* growth conditions. For example, absence of the biological activity of certain enzymes involved in bacterial cell wall synthesis can result in the lysis of cells under normal osmotic conditions, even though protoplasts can be maintained under controlled osmotic conditions. Preferably, but not necessarily, if such a gene is inhibited, e.g., with an antibacterial agent or a phage product, the growth rate of the inhibited bacteria will be less than 50%, more preferably less than 30%, still more preferably less than 20%, and most preferably less than 10% of the growth rate of the uninhibited bacteria. As recognized by those skilled in the art, the degree of growth inhibition will generally depend on the concentration of the inhibitory agent. In the context of the invention, essential genes are generally the preferred targets of antimicrobial agents. Essential genes can encode target molecules directly or can encode a product involved in the production, modification, or maintenance of a target molecule.

A “target” refers to a biomolecule that can be acted on by an exogenous agent, thereby modulating, preferably inhibiting, growth or viability of a cell. In most cases such a target will be a nucleic acid sequence or molecule, or a polypeptide or protein. However, other types of biomolecules can also be targets, e.g., membrane lipids and cell wall structural components.

The term “bacterium” refers to a single bacterial strain, and includes a single cell, and a plurality or population of cells of that strain unless clearly indicated to the contrary. In reference to bacteria or bacteriophage, the term “strain” refers to bacteria or phage having a particular genetic content. The genetic content includes genomic content as well as recombinant vectors. Thus, for example, two otherwise identical bacterial cells would represent different strains if each contained a vector, e.g., a plasmid, with different phage ORF inserts.

In the context of the phage nucleic acid sequences, e.g., gene sequences, of this invention, the terms “homolog” and “homologous” denote nucleotide sequences from different bacteria or phage strains or species or from other types of organisms that have significantly related nucleotide sequences, and consequently significantly

related encoded gene products, preferably having related function. Homologous gene sequences or coding sequences have at least 70% sequence identity (as defined by the maximal base match in a computer-generated alignment of two or more nucleic acid sequences) over at least one sequence window of 48 nucleotides, more preferably at least 80 or 85%, still more preferably at least 90%, and most preferably at least 95%. The polypeptide products of homologous genes have at least 35% amino acid sequence identity over at least one sequence window of 18 amino acid residues, more preferably at least 40%, still more preferably at least 50% or 60%, and most preferably at least 70%, 80%, or 90%. Preferably, the homologous gene product is also a functional homolog, meaning that the homolog will functionally complement one or more biological activities of the product being compared. For nucleotide or amino acid sequence comparisons where a homology is defined by a % sequence identity, the percentage is determined using BLAST programs (with default parameters (Altschul et al., 1997, "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs, *Nucleic Acid Res.* 25:3389-3402). Any of a variety of algorithms known in the art which provide comparable results can also be used, preferably using default parameters. Performance characteristics for three different algorithms in homology searching is described in Salamov et al., 1999, "Combining sensitive database searches with multiple intermediates to detect distant homologues." *Protein Eng.* 12:95-100. Another exemplary program package is the GCG™ package from the University of Wisconsin.

Homologs may also or in addition be characterized by the ability of two complementary nucleic acid strands to hybridize to each other under appropriately stringent conditions. Hybridizations are typically and preferably conducted with probe-length nucleic acid molecules, preferably 20-100 nucleotides in length. Those skilled in the art understand how to estimate and adjust the stringency of hybridization conditions such that sequences having at least a desired level of complementarity will stably hybridize, while those having lower complementarity will not. For examples of hybridization conditions and parameters, see, *e.g.*, Maniatis, T. et al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor University Press, Cold Spring, N.Y.; Ausubel, F.M. et al. (1994) Current Protocols in Molecular Biology. John Wiley & Sons, Secaucus, N.J. Homologs and homologous gene sequences may thus be identified using any nucleic acid sequence

of interest, including the phage ORFs and bacterial target genes of the present invention.

A typical hybridization, for example, utilizes, besides the labeled probe of interest, a salt solution such as 6X SSC (NaCl and Sodium Citrate base) to stabilize nucleic acid strand interaction, a mild detergent such as 0.5% SDS, together with other typical additives such as Denhardt's solution and salmon sperm DNA. The solution is added to the immobilized sequence to be probed and incubated at suitable temperatures to preferably permit specific binding while minimizing nonspecific binding. The temperature of the incubations and ensuing washes is critical to the success and clarity of the hybridization. Stringent conditions employ relatively higher temperatures, lower salt concentrations, and/or more detergent than do non-stringent conditions. Hybridization temperatures also depend on the length, complementarity level, and nature (i.e., "GC content") of the sequences to be tested. Typical stringent hybridizations and washes are conducted at temperatures of at least 40°C, while lower stringency hybridizations and washes are typically conducted at 37°C down to room temperature (~25°C). One of ordinary skill in the art is aware that these conditions may vary according to the parameters indicated above, and that certain additives such as formamide and dextran sulphate may also be added to affect the conditions.

By "stringent hybridization conditions" is meant hybridization conditions at least as stringent as the following: hybridization in 50% formamide, 5X SSC, 50 mM NaH₂PO₄, pH 6.8, 0.5% SDS, 0.1 mg/mL sonicated salmon sperm DNA, and 5X Denhart's solution at 42°C overnight; washing with 2X SSC, 0.1% SDS at 45°C; and washing with 0.2X SSC, 0.1% SDS at 45°C.

Homologous nucleotide sequences will distinguishably hybridize with a reference sequence with up to three mismatches in ten (i.e., at least 70% base match in two sequences of equal length). Preferably, the allowable mismatch level is up to two mismatches in 10, or up to one mismatch in ten, more preferably up to one mismatch in twenty. (Those ratios can, of course, be applied to larger sequences.)

Preferred embodiments involve identification of binding between ORF product and bacterial cellular component that include methods for distinguishing bound molecules, for example, affinity chromatography, immunoprecipitation, crosslinking, and/or genetic screen methods that permit protein:protein interactions to be monitored. One of skill in the art is familiar with these techniques and common

materials utilized (see, *e.g.*, Coligan, J. et al. (eds.) (1995) Current Protocols in Protein Science, John Wiley & Sons, Secaucus, N.J.).

Genetic screening for the identification of protein:protein interactions typically involves the co-introduction of both a chimeric bait nucleic acid sequence (here, the phage ORF to be tested) and a chimeric target nucleic acid sequence that, when co-expressed and having affinity for one another in a host cell, stimulate reporter gene expression to indicate the relationship. A “positive” can thus suggest a potential inhibitory effect in bacteria. This is discussed in further detail in the Detailed Description section below. In this way, new bacterial targets can be identified that are inhibited by specific phage ORF products or derivatives, fragments, mimetics, or other molecules.

Other embodiments involve the identification and/or utilization of a target which is mutated at the site of phage 77 protein interaction but still functional in the cell by virtue of their host’s relatively unresponsive nature in the presence of expression of ORFs previously identified as inhibitory to the non-mutant or wild-type strain. Such mutants have the effect of protecting the host from an inhibition that would otherwise occur (*e.g.*, by competing for binding with the phage ORF product) and indirectly allow identification of the precise responsible target. The identified target can then be used, *e.g.*, for follow-up studies and anti-microbial development. In certain embodiments, rescue from inhibition occurs under conditions in which a bacterial target or mutant target is highly expressed. This is performed, for example, through coupling of the sequence with regulatory element promoters, *e.g.*, as known in the art, which regulate expression at levels higher than wild-type, *e.g.*, at a level sufficiently higher that the inhibitor can be competitively bound to the highly expressed target such that the bacterium is detectably less inhibited.

Identification of the bacterial target can involve identification of a phage-specific site of action. This can involve a newly identified target, or a target where the phage site of action differs from the site of action of a previously known antibacterial agent or inhibitor. For example, phage T7 genes 0.7 and 2.0 target the host RNA polymerase, which is also the cellular target for the antibacterial agent, rifampin. To the extent that a phage product is found to act at a different site than previously described inhibitors, aspects of the present invention can utilize those new, phage-specific sites for identification and use of new agents. The site of action

can be identified by techniques known to those skilled in the art, for example, by mutational analysis, binding competition analysis, and/or other appropriate techniques.

Once a bacterial host target or mutant target sequence has been identified, it too can be conveniently sequenced, sequence analyzed (*e.g.*, by computer), and the underlying gene(s), and corresponding translated product(s) further characterized. Preferred embodiments include such analysis and identification. Preferably such a target has not previously been identified as an appropriate target for antibacterial action.

Also in preferred embodiments in which the bacterial target is a polypeptide or nucleic acid molecule, the identification of a bacterial target of a phage ORF product or fragment includes identification of a cellular and/or biochemical function of the bacterial target. As understood by those skilled in the art, this can, for example, include identification of function by identification of homologous polypeptides or nucleic acid molecules having known function, or identification of the presence of known motifs or sequences corresponding to known function. Such identifications can be readily performed using sequence comparison computer software, such as the BLAST programs and similar other programs and sequence and motif databases.

In embodiments involving expression of a phage ORF in a bacterial strain, in preferred embodiments that expression is inducible. By “inducible” is meant that expression is absent or occurs at a low level until the occurrence of an appropriate environmental stimulus provides otherwise. For the present invention such induction is preferably controlled by an artificial environmental change, such as by contacting a bacterial strain population with an inducing compound (*i.e.*, an inducer). However, induction could also occur, for example, in response to build-up of a compound produced by the bacteria in the bacterial culture, *e.g.*, in the medium. As uncontrolled or constitutive expression of inhibitory ORFs can severely compromise bacteria to the point of eradication, such expression is therefore undesirable in many cases because it would prevent effective evaluation of the strain and inhibitor being studied. For example, such uncontrolled expression could prevent any growth of the strain following insertion of a recombinant ORF, thus preventing determination of effective transfection or transformation. A controlled or inducible expression is therefore advantageous and is generally provided through the provision of suitable regulatory elements, *e.g.*, promoter/operator sequences that can

be conveniently transcriptionally linked to a coding sequence to be evaluated. In most cases, the vector will also contain sequences suitable for efficient replication of the vector in the same or different host cells and/or sequences allowing selection of cells containing the vector, *i.e.*, “selectable markers.” Further, preferred vectors
5 include convenient primer sequences flanking the cloning region from which PCR and/or sequencing may be performed. In preferred embodiments where the purification of phage product is desired, preferably the bacterium or other cell type does not produce a target for the inhibitory product, or is otherwise resistant to the inhibitory product.

10 In preferred embodiments, the target of the phage ORF product or fragment is identified from a bacterial animal pathogen, preferably a mammalian pathogen, more preferably a human pathogen, and is preferably a gene or gene product of such a pathogen. Also in preferred embodiments, the target is a gene or gene product, where the sequence of the target is homologous to a gene or gene product from such
15 a pathogen as identified above.

As used herein, the term “mammal” has its usual biological meaning, and particularly includes bovines, swine, dogs, cats, and humans.

Other aspects of the invention provide isolated, purified, or enriched specific phage nucleic acid and amino acid sequences, subsequences, and homologs thereof
20 from or corresponding to ORFs 17, 19, 43, 102, 104, and 182 from bacteriophage 77 (*Staphylococcus aureus* host bacterium). Such nucleotide sequences are at least 15 nucleotides in length, preferably at least 18, 21, 24, or 27 nucleotides in length, more preferably at least 30, 50, or 90 nucleotides in length. In certain embodiments, longer nucleic acids are preferred, for example those of at least 120, 150, 200, 300,
25 600, 900 or more nucleotides. Such sequences can, for example, be amplification oligonucleotides (*e.g.*, PCR primers), oligonucleotide probes, sequences encoding a portion or all of a phage-encoded protein, or a fragment or all of a phage-encoded protein. In preferred embodiments, the nucleic acid sequence or amino acid
30 sequence contains a sequence which has a lower length as specified above, and an upper-length limit which is no more than 50, 60, 70, 80, or 90% of the length of the full-length ORF or ORF product. The upper-length limit can also be expressed in terms of the number of base pairs of the ORF (coding region).

As it is recognized that alternate codons will encode the same amino acid for most amino acids due to the degeneracy of the genetic code, the sequences of this

aspect includes nucleic acid sequences utilizing such alternate codon usage for one or more codons of a coding sequence. For example, all four nucleic acid sequences GCT, GCC, GCA, and GCG encode the amino acid, alanine. Therefore, if for an amino acid there exists an average of three codons, a polypeptide of 100 amino acids in length will, on average, be encoded by 3^{100} , or 5×10^{47} , nucleic acid sequences. Thus, a nucleic acid sequence can be modified (*e.g.*, a nucleic acid sequence from a phage as specified above) to form a second nucleic acid sequence encoding the same polypeptide as encoded by the first nucleic acid sequence using routine procedures and without undue experimentation. Thus, all possible nucleic acid sequences that encode the amino acid sequences encoded by the phage 77 ORFs 17, 19, 43, 102, 104, and 182, as if all were written out in full, taking into account the codon usage, especially that preferred in the host bacterium.

The alternate codon descriptions are available in common textbooks, for example, Stryer, BIOCHEMISTRY 3rd ed., and Lehninger, BIOCHEMISTRY 3rd ed. Codon preference tables for various types of organisms are available in the literature. Because of the number of sequence variations involving alternate codon usage, for the sake of brevity, individual sequences are not separately listed herein. Instead the alternate sequences are described by reference to the natural sequence with replacement of one or more (up to all) of the degenerate codons with alternate codons from the alternate codon table (Table 2), preferably with selection according to preferred codon usage for the normal host organism or a host organism in which a sequence is intended to be expressed. Those skilled in the art also understand how to alter the alternate codons to be used for expression in organisms where certain codons code differently than shown in the "universal" codon table.

For amino acid sequences, sequences contain at least 5 peptide-linked amino acid residues, and preferably at least 6, 7, 10, 15, 20, 30, or 40, amino acids having identical amino acid sequence as the same number of contiguous amino acid residues in a phage ORF 17, 19, 43, 102, 104, or 182 product. In some cases longer sequences may be preferred, for example, those of at least 50, 70, or 100 amino acids in length. In preferred embodiments, the sequence has bacteria-inhibiting function when expressed or otherwise present in a bacterial cell which is a host for the bacteriophage from which the sequence was derived.

By "isolated" in reference to a nucleic acid is meant that a naturally occurring sequence has been removed from its normal cellular (*e.g.*, chromosomal)

environment or is synthesized in a non-natural environment (*e.g.*, artificially synthesized). Thus, the sequence may be in a cell-free solution or placed in a different cellular environment. The term does not imply that the sequence is the only nucleotide chain present, but that it is essentially free (about 90-95% pure at least) of non-nucleotide material naturally associated with it, and thus is distinguished from isolated chromosomes.

The term "enriched" means that the specific DNA or RNA sequence constitutes a significantly higher fraction (2-5 fold) of the total DNA or RNA present in the cells or solution of interest than in normal or diseased cells or in cells from which the sequence was originally taken. This could be caused by a person by preferential reduction in the amount of other DNA or RNA present, or by a preferential increase in the amount of the specific DNA or RNA sequence, or by a combination of the two. However, it should be noted that enriched does not imply that there are no other DNA or RNA sequences present, just that the relative amount of the sequence of interest has been significantly increased.

The term "significant" is used to indicate that the level of increase is useful to the person making such an increase and an increase relative to other nucleic acids of about at least 2-fold, more preferably at least 5- to 10-fold or even more. The term also does not imply that there is no DNA or RNA from other sources. The other source DNA may, for example, comprise DNA from a yeast or bacterial genome, or a cloning vector such as pUC19. This term distinguishes from naturally occurring events, such as viral infection, or tumor type growths, in which the level of one mRNA may be naturally increased relative to other species of mRNA. That is, the term is meant to cover only those situations in which a person has intervened to elevate the proportion of the desired nucleic acid.

It is also advantageous for some purposes that a nucleotide sequence be in purified form. The term "purified" in reference to nucleic acid does not require absolute purity (such as a homogeneous preparation). Instead, it represents an indication that the sequence is relatively more pure than in the natural environment (compared to the natural level, this level should be at least 2-5 fold greater, *e.g.*, in terms of mg/mL). Individual clones isolated from a genomic or cDNA library may be purified to electrophoretic homogeneity. The claimed DNA molecules obtained from these clones could be obtained directly from total DNA or from total RNA. cDNA clones are not naturally occurring, but rather are preferably obtained via

manipulation of a partially purified naturally occurring substance (messenger RNA). The construction of a cDNA library from mRNA involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection of the cells carrying the cDNA library. Thus, the process which includes the construction of a cDNA library from mRNA and isolation of distinct cDNA clones yields an approximately 10^6 -fold purification of the native message. Thus, purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated. A genomic library can be used in the same way and yields the same approximate levels of purification.

The terms "isolated", "enriched", and "purified" with respect to the nucleic acids, above, may similarly be used to denote the relative purity and abundance of polypeptides (multimers of amino acids joined one to another by α -carboxyl: α -amino group (peptide) bonds). These, too, may be stored in, grown in, screened in, and selected from libraries using biochemical techniques familiar in the art. Such polypeptides may be natural, synthetic or chimeric and may be extracted using any of a variety of methods, such as antibody immunoprecipitation, other "tagging" techniques, conventional chromatography and/or electrophoretic methods. Some of the above utilize the corresponding nucleic acid sequence.

As indicated above, aspects and embodiments of the invention are not limited to entire genes and proteins. The invention also provides and utilizes fragments and portions thereof, preferably those which are "active" in the inhibitory sense described above. Such peptides or oligopeptides and oligo or polynucleotides have preferred lengths as specified above for nucleic acid and amino acid sequences from phage; corresponding recombinant constructs can be made to express the encoded same. Also included are homologous sequences and fragments thereof.

The nucleotide and amino acid sequences identified herein are believed to be correct, however, certain sequences may contain a small percentage of errors, *e.g.*, 1-5%. In the event that any of the sequences have errors, the corrected sequences can be readily provided by one skilled in the art using routine methods. For example, the nucleotide sequences can be confirmed or corrected by obtaining and culturing the relevant phage, and purifying phage genomic nucleic acids. A region or regions of interest can be amplified, *e.g.*, by PCR from the appropriate genomic template, using primers based on the described sequence. The amplified regions can then be

sequenced using any of the available methods (*e.g.*, a dideoxy termination method, for example, using commercially available products). This can be done redundantly to provide the corrected sequence or to confirm that the described sequence is correct. Alternatively, a particular sequence or sequences can be identified and
5 isolated as an insert or inserts in a phage genomic library and isolated, amplified, and sequenced by standard methods. Confirmation or correction of a nucleotide sequence for a phage gene provides an amino acid sequence of the encoded product by merely reading off the amino acid sequence according to the normal codon relationships and/or expressed in a standard expression system and the polypeptide
10 product sequenced by standard techniques. The sequences described herein thus provide unique identification of the corresponding genes and other sequences, allowing those sequences to be used in the various aspects of the present invention. Confirmation of a phage ORF encoded amino acid sequence can also be confirmed by constructing a recombinant vector from which the ORF can be expressed in an
15 appropriate host (*e.g.*, *E. coli*), purified, and sequenced by conventional protein sequencing methods.

In other aspects the invention provides recombinant vectors and cells harboring phage 77 ORF 17, 19, 43, 102, 104, or 182 or portions thereof, or bacterial target sequences described herein, preferably where the phage or bacterial sequence
20 is inserted in a recombinant vector. As understood by those skilled in the art, vectors may assume different forms, including, for example, plasmids, cosmids, and virus-based vectors. See, *e.g.*, Maniatis, T. et al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor University Press, Cold Spring, N.Y.; See also, Ausubel, F.M. et al. (eds.) (1994) Current Protocols in Molecular Biology.
25 John Wiley & Sons, Secaucus, N.J.

In preferred embodiments, the vectors will be expression vectors, preferably shuttle vectors that permit cloning, replication, and expression within bacteria. An “expression vector” is one having regulatory nucleotide sequences containing transcriptional and translational regulatory information that controls expression of
30 the nucleotide sequence in a host cell. Preferably the vector is constructed to allow amplification from vector sequences flanking an insert locus. In certain embodiments, the expression vectors may additionally or alternatively support expression, and/or replication in animal, plant and/or yeast cells due to the presence of suitable regulatory sequences, *e.g.*, promoters, enhancers, 3’ stabilizing

sequences, primer sequences, etc. In preferred embodiments, the promoters are inducible and specific for the system in which expression is desired, *e.g.*, bacteria, animal, plant, or yeast. The vectors may optionally encode a “tag” sequence or sequences to facilitate protein purification or protein detection. Convenient
5 restriction enzyme cloning sites and suitable selective marker(s) are also optionally included. Such selective markers can be, for example, antibiotic resistance markers or markers which supply an essential nutritive growth factor to an otherwise deficient mutant host, *e.g.*, tryptophan, histidine, or leucine in the Yeast Two-Hybrid systems described below.

10 The term “recombinant vector” relates to a single- or double-stranded circular nucleic acid molecule that can be transfected into cells and replicated within or independently of a cell genome. A circular double-stranded nucleic acid molecule can be cut and thereby linearized upon treatment with appropriate restriction enzymes. An assortment of nucleic acid vectors, restriction enzymes, and the
15 knowledge of the nucleotide sequences cut by restriction enzymes are readily available to those skilled in the art. A nucleic acid molecule encoding a desired product can be inserted into a vector by cutting the vector with restriction enzymes and ligating the two pieces together. Preferably the vector is an expression vector, *e.g.*, a shuttle expression vector as described above.

20 By “recombinant cell” is meant a cell possessing introduced or engineered nucleic acid sequences, *e.g.*, as described above. The sequence may be in the form of or part of a vector or may be integrated into the host cell genome. Preferably the cell is a bacterial cell.

In preferred embodiments, the inserted nucleic acid sequence corresponding to
25 at least a portion of a bacteriophage 77 ORF 17, 19, 43, 102, 104, and 182 gene product has a length as specified for the isolated purified or enriched nucleic acid sequences in an aspect above.

In another aspect, the invention also provides methods for identifying and/or screening compounds “active on” at least one bacterial target of a bacteriophage
30 inhibitor protein or RNA. Preferred embodiments involve contacting bacterial target proteins with a test compound, and determining whether the compound binds to or reduces the level of activity of the bacterial target, *e.g.*, a bacterial protein. Preferably this is done *in vivo* under approximately physiological conditions. The compounds that can be used may be large or small, synthetic or natural, organic or

inorganic, proteinaceous or non-proteinaceous. In preferred embodiments, the compound is a peptidomimetic, as described herein, a bacteriophage inhibitor protein or fragment or derivative thereof, preferably an “active portion”, or a small molecule. In particular embodiments, the methods include the identification of
5 bacterial targets as described above or otherwise described herein. Preferably the fragment of a bacteriophage inhibitor protein includes less than 80% of an intact bacteriophage inhibitor protein. Preferably, the at least one target includes a plurality of different targets of bacteriophage inhibitor proteins, preferably a plurality of different targets. The plurality of targets can be in or from a plurality of
10 different bacteria, but preferably is from a single bacterial species.

In embodiments involving binding assays, preferably binding is to a fragment or portion of a bacterial target protein, where the fragment includes less than 90%, 80%, 70%, 60%, 50%, 40%, or 30% of an intact bacterial target protein. Preferably, the at least one bacterial target includes a plurality of different targets of
15 bacteriophage inhibitor proteins, preferably a plurality of different targets. The plurality of targets can be in or from a plurality of different bacteria, but preferably is from a single bacterial species.

A “method of screening” refers to a method for evaluating a relevant activity or property of a large plurality of compounds, rather than just one or a few
20 compounds. For example, a method of screening can be used to conveniently test at least 100, more preferably at least 1000, still more preferably at least 10,000, and most preferably at least 100,000 different compounds, or even more.

In the context of this invention, the term “small molecule” refers to compounds having molecular mass of less than 3000 Daltons, preferably less than
25 2000 or 1500, still more preferably less than 1000, and most preferably less than 600 Daltons. Preferably but not necessarily, a small molecule is not an oligopeptide.

In a related aspect or in preferred embodiments, the invention provides a method of screening for potential antibacterial agents by determining whether any of a plurality of compounds, preferably a plurality of small molecules, is active on at
30 least one target of a bacteriophage inhibitor protein or RNA. Preferred embodiments include those described for the above aspect, including embodiments which involve determining whether one or more test compounds bind to or reduce the level of activity of a bacterial target, and embodiments which utilize a plurality of different targets as described above.

The identification of bacteria-inhibiting phage ORFs and their encoded products also provides a method for identifying an active portion of such an encoded product. This also provides a method for identifying a potential antibacterial agent by identifying such an active portion of a phage ORF or ORF product. In preferred
5 embodiments, the identification of an active portion involves one or more of mutational analysis, deletion analysis, or analysis of fragments of such products. The method can also include determination of a 3-dimensional structure of an active portion, such as by analysis of crystal diffraction patterns. In further embodiments, the method involves constructing or synthesizing a peptidomimetic compound,
10 where the structure of the peptidomimetic compound corresponds to the structure of the active portion.

In this context, “corresponds” means that the peptidomimetic compound structure has sufficient similarities to the structure of the active portion that the peptidomimetic will interact with the same molecule as the phage protein and
15 preferably will elicit at least one cellular response in common which relates to the inhibition of the cell by the phage protein.

The methods for identifying or screening for compounds or agents active on a bacterial target of a phage-encoded inhibitor can also involve identification of a phage-specific site of action on the target.

20 An “active portion” as used herein denotes an epitope, a catalytic or regulatory domain, or a fragment of a bacteriophage inhibitor protein that is responsible for, or a significant factor in, bacterial target inhibition. The active portion preferably may be removed from its contiguous sequences and, in isolation, still effect inhibition.

By “mimetic” is meant a compound structurally and functionally related to a
25 reference compound that can be natural, synthetic, or chimeric. In terms of the present invention, a “peptidomimetic,” for example, is a compound that mimics the activity-related aspects of the 3-dimensional structure of a peptide or polypeptide in a non-peptide compound, for example mimics the structure of a peptide or active portion of a phage- or bacterial ORF-encoded polypeptide.

30 A related aspect provides a method for inhibiting a bacterial cell by contacting the bacterial cell with a compound active on a bacterial target of a bacteriophage inhibitor protein or RNA encoded by bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182, where the target was uncharacterized. In preferred embodiments, the compound is such a protein, or a fragment or derivative thereof; a structural mimetic,

e.g., a peptidomimetic, of such a protein or fragment; a small molecule; the contacting is performed *in vitro*, the contacting is performed *in vivo* in an infected or at risk organism, e.g., an animal such as a mammal or bird, for example, a human, or other mammal described herein, or in a plant.

5 In the context of this invention, the term “bacteriophage inhibitor protein” refers to a protein encoded by a bacteriophage nucleic acid sequence which inhibits bacterial function in a host bacterium. Thus, it is a bacteria-inhibiting phage product.

10 In the context of this invention, the phrase “contacting the bacterial cell with a compound active on a bacterial target of a bacteriophage inhibitor protein” or equivalent phrases refer to contacting with an isolated, purified, or enriched compound or a composition including such a compound, but specifically does not rely on contacting the bacterial cell with an intact naturally occurring phage which encodes the compound. Preferably no intact phage are involved in the contacting.

15 Related aspects provide methods for prophylactic or therapeutic treatment of a bacterial infection by administering to an infected, challenged or at risk organism a therapeutically or prophylactically effective amount of a compound active on a target of a bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182 product, e.g., as described for the previous aspect. Preferably the bacterium involved in the infection
20 or risk of infection produces the identified target of the bacteriophage inhibitor protein or alternatively produces a homologous target compound. In preferred embodiments, the host organism is a plant or animal, preferably a mammal or bird, and more preferably, a human or other mammal described herein. Preferred embodiments include, without limitation, those as described for the preceding
25 aspect.

30 Compounds useful for the methods of inhibiting, methods of treating, and pharmaceutical compositions can include novel compounds, but can also include compounds which had previously been identified for a purpose other than inhibition of bacteria. Such compounds can be utilized as described and can be included in pharmaceutical compositions.

By “treatment” or “treating” is meant administering a compound or pharmaceutical composition for prophylactic and/or therapeutic purposes. The term “prophylactic treatment” refers to treating a patient or animal that is not yet infected but is susceptible to or otherwise at risk of a bacterial infection. The term

“therapeutic treatment” refers to administering treatment to a patient already suffering from infection.

The term “bacterial infection” refers to the invasion of the host organism, animal or plant, by pathogenic bacteria. This includes the excessive growth of bacteria which are normally present in or on the body of the organism, but more generally, a bacterial infection can be any situation in which the presence of a bacterial population(s) is damaging to a host organism. Thus, for example, an organism suffers from a bacterial infection when excessive numbers of a bacterial population are present in or on the organism’s body, or when the effects of the presence of a bacterial population(s) is damaging to the cells, tissue, or organs of the organism.

The terms “administer”, “administering”, and “administration” refer to a method of giving a dosage of a compound or composition, *e.g.*, an antibacterial pharmaceutical composition, to an organism. Where the organism is a mammal, the method is, *e.g.*, topical, oral, intravenous, transdermal, intraperitoneal, intramuscular, or intrathecal. The preferred method of administration can vary depending on various factors, *e.g.*, the components of the pharmaceutical composition, the site of the potential or actual bacterial infection, the bacterium involved, and the infection severity.

The term “mammal” has its usual biological meaning, referring to any organism of the Class Mammalia of higher vertebrates that nourish their young with milk secreted by mammary glands, *e.g.*, mouse, rat, and, in particular, human, bovine, sheep, swine, dog, and cat.

In the context of treating a bacterial infection a “therapeutically effective amount” or “pharmaceutically effective amount” indicates an amount of an antibacterial agent, *e.g.*, as disclosed for this invention, which has a therapeutic effect. This generally refers to the inhibition, to some extent, of the normal cellular functioning of bacterial cells that renders or contributes to bacterial infection.

The dose of antibacterial agent that is useful as a treatment is a “therapeutically effective amount.” Thus, as used herein, a therapeutically effective amount means an amount of an antibacterial agent that produces the desired therapeutic effect as judged by clinical trial results and/or animal models. This amount can be routinely determined by one skilled in the art and will vary depending

on several factors, such as the particular bacterial strain involved and the particular antibacterial agent used.

In connection with claims to methods of inhibiting bacteria and therapeutic or prophylactic treatments, “a compound active on a target of a bacteriophage inhibitor protein” or terms of equivalent meaning differ from administration of or contact with an intact phage naturally encoding the full-length inhibitor compound. While an intact phage may conceivably be incorporated in the present methods, the method at least includes the use of an active compound as specified different from a full length inhibitor protein naturally encoded by a bacteriophage and/or a delivery or contacting method different from administration of or contact with an intact phage naturally encoding the full-length protein. Similarly, pharmaceutical compositions described herein at least include an active compound or composition different from a phage naturally coding the full-length inhibitor protein, or such a full-length protein is provided in the composition in a form different from being encoded by an intact phage. Preferably the methods and compositions do not include an intact phage.

In accordance with the above aspects, the invention also provides antibacterial agents and compounds active on a bacterial target of bacteriophage ORF 17, 19, 43, 102, 104, or 182, where the target was uncharacterized as indicated above. As previously indicated, such active compounds include both novel compounds and compounds which had previously been identified for a purpose other than inhibition of bacteria. Such previously identified biologically active compounds can be used in embodiments of the above methods of inhibiting and treating. In preferred embodiments, the targets, bacteriophage, and active compound are as described herein for methods of inhibiting and methods of treating. Preferably the agent or compound is formulated in a pharmaceutical composition which includes a pharmaceutically acceptable carrier, excipient, or diluent. In addition, the invention provides agents, compounds, and pharmaceutical compositions where an active compound is active on an uncharacterized phage-specific site on the target.

In preferred embodiments, the target is as described for embodiments of aspects above.

Likewise, the invention provides a method of making an antibacterial agent. The method involves identifying a target of a bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182 product, screening a plurality of compounds to identify a compound active on the target, and synthesizing the compound in an amount sufficient to

provide a therapeutic effect when administered to an organism infected by a bacterium naturally producing the target.

In preferred embodiments, the identification of the target and identification of active compounds include steps or methods and/or components as described above (or otherwise herein) for such identification. Likewise, the active compound can be as described above, including fragments and derivatives of phage inhibitor proteins, peptidomimetics, and small molecules. As recognized by those skilled in the art, peptides can be synthesized by expression systems and purified, or can be synthesized artificially by methods well known in the art.

In the context of nucleic acid or amino acid sequences of this invention, the term "corresponding" indicates that the sequence is at least 95% identical, preferably at least 97% identical, and more preferably at least 99% identical to a sequence from the specified phage genome or bacterial genome, a ribonucleotide equivalent, a degenerate equivalent (utilizing one or more degenerate codons), or a homologous sequence, where the homolog provides functionally equivalent biological function.

In embodiments where the bacterial target of a bacteriophage inhibitor ORF product, e.g., an inhibitory protein or polypeptide, the target is preferably encoded by a *S. aureus* nucleic acid coding sequence from a host bacterium for bacteriophage 77. Target sequences are described herein by reference to sequence source sites.

The sequence encoding the target preferably corresponds to a *S. aureus* nucleic acid sequence available from numerous sources including *S. aureus* sequences deposited in GenBank, *S. aureus* sequences found in European Patent Application No. 97100110.7 to Human Genome Sciences, Inc. filed January 7, 1997, *S. aureus* sequences available from TIGR at <http://www.tigr.org/tdb/mdb/mdb.html>, and *S. aureus* sequences available from the Oklahoma University *S. aureus* sequencing project at the following URL: http://www.genome.ou.edu/staph_new.html.

The amino acid sequence of a polypeptide target is readily provided by translating the corresponding coding region. For the sake of brevity, the sequences are not reproduced herein. Also, in preferred embodiments, a target sequence corresponds to a *S. aureus* coding sequences corresponding to a sequence listed in Table 6 herein. The listing in Table 6 describes *S. aureus* sequences currently deposited in GenBank. Again, for the sake of brevity, the sequences are described by reference to the GenBank entries instead of being written out in full herein. In cases where an entry for a coding region is not complete, the complete sequence can

be readily obtained by routine methods, e.g., by isolating a clone in a phage 77 host *S. aureus* genomic library, and sequencing the clone insert to provide the relevant coding region. The boundaries of the coding region can be identified by conventional sequence analysis and/or by expression in a bacterium in which the endogenous copy of the coding region has been inactivated and using subcloning to identify the functional start and stop codons for the coding region.

As used in the claims to describe the various inventive aspects and embodiments, "comprising" means including, but not limited to, whatever follows the word "comprising". Thus, use of the term "comprising" indicates that the listed elements are required or mandatory, but that other elements are optional and may or may not be present. By "consisting of" is meant including, and limited to, whatever follows the phrase "consisting of". Thus, the phrase "consisting of" indicates that the listed elements are required or mandatory and that no other elements may be present. By "consisting essentially of" is meant including any elements listed after the phrase, and limited to other elements that do not interfere with or contribute to the activity or action specified in the disclosure for the listed elements. Thus, the phrase "consisting essentially of" indicates that the listed elements are required or mandatory, but that other elements are optional and may or may not be present depending upon whether or not they affect the activity or action of the listed elements.

Additional features and embodiments of the present invention will be apparent from the following Detailed Description and from the claims, all within the scope of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a flow schematic showing the manipulations necessary to convert pT0021, an arsenite inducible vector containing the luciferase gene, into pTHA or pTM, two *ars* inducible vectors. Vector pTHA contains BamH I, Sal I, and Hind III cloning sites and a downstream HA epitope tag. Vector pTM contains Bam HI and Hind III cloning sites and no HA epitope tag.

FIGURE 2 is a schematic representation of the cloning steps involved to place the DNA segments of any of ORFs 17/ 19/ 43/ 102/104/182 or other sequences into pTHA to assess inhibitory potential. For subcloning into pTM or pT0021, Individual ORFs were amplified by the PCR using oligonucleotides targeting the ATG and stop codons of the ORFs. Using this strategy, Bam HI and Hind III sites were positioned immediately upstream or downstream, respectively of the start and stop codons of each ORF. Following digestion with Bam HI and Hind III, the PCR fragments were subcloned into the same sites of pT0021 or pTM. Clones were verified by PCR and direct sequencing.

- FIGURE 3 shows a schematic representation of the functional assays used to characterize the bactericidal and bacteriostatic potential of all predicted ORFs (>33 amino acids) encoded by bacteriophage 77. Fig. 3A) Functional assay on semi-solid support media. Fig. 3B) Functional assay in liquid culture.
- FIGURE 4 shows the results of a screen to assess killing potential of bacteriophage 77 encoded ORFs (>33 amino acids) on semi-solid support media. For each ORF tested between one to three independent transformants were tested at two different concentrations. Each panel (A-H) consists of 3 sections: I) A grid showing the position of spotting of individual *Staphylococcus aureus* transformant clones containing a given ORF. The number on the grid refers to the ORF contained within a given Staph A. clone and the number following the dash identifies the different transformants. For example, 5-3 and 5-1 refers to ORF 5, transformant #3 and ORF 5, transformant #1, respectively. A full darkened bar under the name of the Staph clone infers that an undiluted sample of the overnight culture was spotted onto the agar plate; whereas a shortened bar indicates that a 10-fold diluted sample of the overnight culture was spotted onto the agar plate. II) An overnight culture of the *Staphylococcus aureus* transformant was spotted onto directly, or after a 10-fold diluted, onto an agar plate lacking arsenite. III) II) An overnight culture of the *Staphylococcus aureus* transformant was spotted onto directly, or after a 10-fold diluted, onto an agar plate containing 5 μ M arsenite, to induce expression of the ars promoter and hence of the bacteriophage 77 ORF. From this experiment, it is clear that expression of bacteriophage ORF 19 (Panel A) and ORF 182 (Panel C) lead to inhibition of growth of *Staphylococcus aureus*. Positive controls for this experiment

included expression of the lysis cassette from bacteriophage 77 (Panel H, Lys-1, Lys-2, Lys-3) and the lysis cassette from bacteriophage 77 (TH-1, TH-2, TH-3).

- FIGURE 5 shows the results of a screen to assess killing potential of bacteriophage 77 encoded ORFs (>33 amino acids) on semi-solid support media. In this experiment, clones of *Staphylococcus aureus* harboring a given bacteriophage 77 ORF were streaked on plates lacking or containing 5 μ M arsenite. Following incubation of the plates at 37°C overnight, inhibition of growth was visually assessed. The identity of the expression vector and subcloned ORF harbored by the *Staphylococcus* transformant is given around the border of each plate. From this experiment, it is clear that expression of bacteriophage ORF 17 (Panel A), ORF 43 (Panel B), ORF 102, (Panel B and C), and ORF 104 (Panel D) lead to inhibition of growth of *Staphylococcus aureus*.
- FIGURE 6 is a bar graph showing the results of a screen in liquid media to assess bacteriostatic or bactericidal activity of 93 predicted ORFs (>33 amino acids) encoded by bacteriophage 77. Growth inhibition assays were performed as detailed in the Detailed Description. The relative growth of *Staphylococcus aureus* transformants harboring a given bacteriophage 77 ORF (identified on the bottom of the graph), in the absence or presence of arsenite, is plotted relative to growth of a *Staphylococcus aureus* transformant containing ORF 5, a non-toxic bacteriophage 77 ORF (which is set at 100%). Each bar represents the average obtained from three *Staph A* transformants grown in duplicate. Bacteriophage 77 ORFs showing significant growth inhibition are plotted in red and consist of ORF 17, 19, 102, 104, and 182.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Preliminarily the tables will be briefly described.

- Table 1 shows the complete nucleotide sequence of the genome of *Staphylococcus aureus* bacteriophage 77.

Table 2 is a table from Alberts et al., MOLECULAR BIOLOGY OF THE CELL 3rd ed., showing the redundancy of the “universal” genetic code.

Table 3 FIGURE 3 shows the predicted nucleotide sequence, predicted amino acid sequence, and physiochemical parameters of ORF 17/ 19/ 43/ 102/ 104/

182]. These include the primary amino acid sequence of the predicted protein, the average molecular weight, amino acid composition, theoretical pI, hydrophobicity map, and predicted secondary structure map.

Table 4 FIGURE 4 Shows homology search results. BLAST analysis was performed with ORFs 17/ 19/ 43/ 102/ 104/ 182 against NCBI non-redundant nucleotide and Swissprot databases. The results of this search indicate that: I) ORF 17 has no significant homology to any gene in the NCBI non-NCBI non-redundant nucleotide database, II) ORF 19 has significant homology to one gene in the NCBI non-redundant nucleotide database - the gene encoding ORF 59 of bacteriophage phi PVL, III) ORF 43 has significant homology to one gene in the NCBI non-redundant nucleotide database - the gene encoding ORF 39 of phi PVL, IV) ORF 102 has significant homology to one gene in the NCBI non-redundant nucleotide database - the gene encoding ORF 38 of phi PVL, V) ORF 104 has no significant homology to any gene in the NCBI non-redundant nucleotide database, VI) ORF 182 has significant homology to one gene in the NCBI non-redundant nucleotide database - the gene encoding ORF 39 of phi PVL.

Table 5 FIGURE 7 shows a list of all the ORFs from Bacteriophage 77 that were screened in the functional assay to identify those with anti-microbial activity.

Table 6 is a list of *Staphylococcus aureus* sequences which may represent genes coding for target sequences for the phage 77-encoded antimicrobial proteins or peptides.

The present invention is based on the identification of naturally-occurring DNA sequence elements encoding RNA or proteins with anti-microbial activity. Bacteriophages or phages, are viruses that infect and kill bacteria. They are natural enemies of bacteria and, over the course of evolution have perfected enzymes (products of DNA sequences) which enable them to infect a host bacteria, replicate their genetic material, usurp host metabolism, and ultimately kill their host. The scientific literature documents well the fact that many known bacteria have a large number of such bacteriophages that can infect and kill them (for example, see the ATCC bacteriophage collection at <http://www.atcc.org>) (Ackermann and DuBow, 1987). Although we know that many bacteriophages encode proteins which can significantly alter their host's metabolism, determination of the killing potential of a

given bacteriophage gene product can only be assessed by expressing the gene product in the target bacterial strain.

As indicated in the Summary above, the present invention is concerned with the use of bacteriophage 77 coding sequences and the encoded polypeptides or RNA transcripts to identify bacterial targets for potential new antibacterial agents. Thus, the invention concerns the selection of relevant bacteria. Particularly relevant bacteria are those which are pathogens of a complex organism such as an animal, *e.g.*, mammals, reptiles, and birds, and plants. However, the invention can be applied to any bacterium (whether pathogenic or not) for which bacteriophage are available or which are found to have cellular components closely homologous to components targeted by phage 77 ORFs 17, 19, 43, 102, 104, and 182.

Identification of ORFs 17, 19, 43, 102, 104, and 182 and products from the phage which inhibit the host bacterium both provides an inhibitor compound and allows identification of the bacterial target affected by the phage-encoded inhibitor. Such a target is thus identified as a potential target for development of other antibacterial agents or inhibitors and the use of those targets to inhibit those bacteria. As indicated above, even if such a target is not initially identified in a particular bacterium, such a target can still be identified if a homologous target is identified in another bacterium. Usually, but not necessarily, such another bacterium would be a genetically closely related bacterium. Indeed, in some cases, an inhibitor encoded by phage 77 ORF 17, 19, 43, 102, 104, or 182 can also inhibit such a homologous bacterial cellular component.

The demonstration that bacteriophage have adapted to inhibiting a host bacterium by acting on a particular cellular component or target provides a strong indication that that component is an appropriate target for developing and using antibacterial agents, *e.g.*, in therapeutic treatments. Thus, the present invention provides additional guidance over mere identification of bacterial essential genes, as the present invention also provides an indication of accessibility of the target to an inhibitor, and an indication that the target is sufficiently stable over time (*e.g.*, not subject to high rates of mutation) as phage acting on that target were able to develop and persist. Thus, the present invention identifies a particular subset of essential cellular components which are particularly likely to be appropriate targets for development of antibacterial agents.

The invention also, therefore, concerns the development or identification of inhibitors of bacteria, in addition to the phage-encoded inhibitory proteins (or RNA transcripts), which are active on the targets of bacteriophage-encoded inhibitors. As described herein, such inhibitors can be of a variety of different types, but are preferably small molecules.

The following description provides preferred methods for implementing the various aspects of the invention. However, as those skilled in the art will readily recognize, other approaches can be used to obtain and process relevant information. Thus, the invention is not limited to the specifically described methods. In addition, the following description provides a set of steps in a particular order. That series of steps describes the overall development involved in the present invention. However, it is clear that individual steps or portions of steps may be usefully practiced separately, and, further, that certain steps may be performed in a different order or even bypassed if appropriate information is already available or is provided by other sources or methods.

Identification of Inhibitory ORF

The methodology previously described in U.S. Provisional Patent Application NO. 60/110,992, and filed December 3, 1998, was used to identify and characterize DNA sequences from *Staphylococcus aureus* bacteriophage 77 that can act as anti-microbials. A nucleic acid segment isolated from *Staphylococcus aureus* bacteriophage 77 encodes a protein, whose gene is referred to as ORF (open reading frame) 17, 19, 43, 102, 104, or 182. Thus, the present invention provides a nucleic acid sequence isolated from *Staphylococcus aureus* (*Staph A* or *S. aureus*) bacteriophage 77 comprising at least a portion of the gene encoding ORF 17, 19, 43, 102, 104, or 182 with anti-microbial activity. The nucleic acid sequence can be isolated using a method similar to those described herein, or using another method. In addition, such a nucleic acid sequence can be chemically synthesized. Having the anti-microbial nucleic acid sequence of the present invention, parts thereof or oligonucleotides derived therefrom, other anti-microbial sequences from other bacteriophage sources using methods described herein or other methods can be isolated, including screening methods based on nucleic acid sequence hybridization.

The present invention provides the use of the *Staph A* bacteriophage 77 anti-microbial DNA segment encoding ORF 17, 19, 43, 102, 104, or 182], as a pharmacological agent – either wholly or in part - as well as the use of

peptidomimetics, developed from amino acid or nucleotide sequence knowledge of *Staph A* bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182. This can be achieved where the structure of the peptidomimetic compound corresponds to the structure of the active portion of ORF 17, 19, 43, 102, 104, or 182. In this analysis, the peptide backbone is transformed into a carbon-based hydrophobic structure that can retain cytostatic or cytotoxic activity for the bacterium. This is done by standard medicinal chemistry methods, measuring growth inhibition of the various molecules in liquid cultures or on solid medium. These mimetics also represent lead compounds for the development of novel antibiotics.

In this context, "corresponds" means that the peptidomimetic compound structure has sufficient similarities to the structure of the active portion of ORF 17, 19, 43, 102, 104, or 182 that the peptidomimetic will interact with the same molecule as the product of ORF 17, 19, 43, 102, 104, or 182 and preferably will elicit at least one cellular response in common which relates to the inhibition of the cell by the phage protein.

The invention also provides bacteriophage anti-microbial DNA segments from other phages based on nucleic acids and sequences hybridizing to the presently identified inhibitory ORF under high stringency conditions or sequences which are homologous as described above. The bacteriophage anti-microbial DNA segment from bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182 can be used to identify a related segment from another related or unrelated phage based on conditions of hybridization or sequence comparison.

Identification of Bacterial Targets

The present invention provides the use of *Staphylococcus* bacteriophage 77 ORFs 17, 19, 43, 102, 104, and 182 anti-microbial activity to identify essential host bacterium interacting proteins or other targets that could, in turn, be used for drug design and/or screening of test compounds. Thus, the invention provides a method of screening for antibacterial agents by determining whether test compounds interact with (e.g., bind to) the bacterial target. The invention also provides a method of making an antibacterial agent based on production and purification of the protein or RNA product of bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182. The method involves identifying a bacterial target of the product of ORF 17, 19, 43, 102, 104, or 182, screening a plurality of compounds to identify a compound active on the target,

and synthesizing the compound in an amount sufficient to provide a therapeutic effect when administered to an organism infected by a bacterium naturally producing the target. The rationale is that the product of ORFs 17, 19, 43, 102, 104, and 182 can physically interact and/or modify certain microbial host components to block their function.

A variety of methods are known to those skilled in the art for identifying interacting molecules and for identifying target cellular components. Several approaches and techniques are described below which can be used to identify the host bacterial pathway and protein that interact or are inhibited by ORF 17, 19, 43, 102, 104, or 182.

The first approach is a genetic screen for protein:protein interaction, e.g., either some form of two hybrid screen or some form of suppressor screen. In one form of the two hybrid screen involving the yeast two hybrid system, the nucleic acid segment encoding ORF 17, 19, 43, 102, 104, or 182], or a portion thereof, is fused to the carboxyl terminus of the yeast Gal4 activation domain II (amino acids 768-881) to create a bait vector. A cDNA library of cloned *S. aureus* sequences which have been engineered into a plasmid where the *S. aureus* sequences are fused to the DNA binding domain of Gal4 is also generated. These plasmids are introduced alone, or in combination, into a yeast strain, e.g., Y190, previously engineered with chromosomally integrated copies of the *E. coli lacZ* and the selectable *His3* genes, both under Gal4 regulation (Durfee et al., 1993). If the two proteins expressed in yeast interact, the resulting complex will activate transcription from promoters containing Gal4 binding sites. A *lacZ* and *His3* gene, each driven by a promoter containing Gal4 binding sites, have been integrated into the genome of the host yeast system and are used for measuring protein-protein interactions. Such a system provides a physiological environment in which to detect potential protein interactions.

This system has been extensively used to identify novel protein-protein interaction partners and to map the sites required for interaction (for example, to identify interacting partners of translation factors (Qui et al., 1998), transcription factors (Katagiri et al., 1998), proteins involved in signal transduction (Endo et al., 1997). Alternatively, a bacterial two-hybrid screen can be utilized to circumvent the need for the interacting proteins to be targeted to the nucleus, as is the case in the yeast system (Karimova et al., 1998).

The protein targets of ORFs 17, 19, 43, 102, 104, and 182 can also be identified using bacterial genetic screens. One approach involves the overexpression of ORF 17, 19, 43, 102, 104, or 182 protein in mutagenized *S. aureus* followed by plating the cells and searching for colonies that can survive the anti-microbial activity of ORF 17, 19, 43, 102, 104, or 182. These colonies are then grown, their DNA extracted, and cloned into an expression vector that contains a replicon of a different incompatibility group from the plasmid expressing ORF 17, 19, 43, 102, 104, or 182. This library is then introduced into a wild-type *Staph A* bacterium in conjunction with an expression vector driving synthesis of ORF 17, 19, 43, 102, 104, or 182, followed by selection for surviving bacteria. Thus, *Staph A* DNA fragments from the survivors presumably contain a DNA fragment from the original mutagenized *Staph A* genome that can protect the cell from the antimicrobial activity of ORF 17, 19, 43, 102, 104, or 182. This fragment can be sequenced and compared with that of the bacterial host to determine in which gene the mutation lies. This approach enables one to determine the targets and pathways that are affected by the killing function.

Alternatively, the bacterial targets can be determined in the absence of selecting for mutations using the approach known as "multicopy suppression". In this approach, the DNA from the wild type *Staph A* host is cloned into an expression vector that can coexist with the one containing ORF 17, 19, 43, 102, 104, or 182. Those plasmids that contain host DNA fragments and genes which protect the host from the anti microbial activity of ORF 17, 19, 43, 102, 104, or 182 can then be isolated and sequenced to identify putative targets and pathways in the host bacteria.

Another approach is based on identifying protein:protein interactions between the product of ORF 17, 19, 43, 102, 104, or 182 and *S. aureus* host proteins, using a biochemical approach based on affinity chromatography. This approach has been used to identify interactions between lambda phage proteins and proteins from their *E. coli* host (Sopta et al., 1995). The product of ORF 17, 19, 43, 102, 104, or 182 is fused to a tag (e.g. -glutathione-S-transferase) after insertion in a commercially available plasmid vector which directs high-level expression after induction of the responsive promoter driving the fusion protein. The fusion protein is expressed in *E. coli*, purified, and immobilized on a solid phase matrix. Total cell extracts from *S. aureus* are then passed through the affinity matrix containing the immobilized phage ORF fusion protein; host proteins retained on the column are

then eluted under different conditions of ionic strength, pH, and detergents and identified by gel electrophoresis. They are recovered from the gel by transfer to a high affinity membrane. The proteins are individually digested to completion with a protease (e.g.-trypsin) and either molecular mass or the amino acid sequence of the tryptic fragments can be determined by mass spectrometry using MALDI-TOF technology (Qin et al., 1997). The sequence of the individual peptides from a single protein are then analyzed by a bioinformatics approach to identify the *S. aureus* protein interacting with the phage ORF. This is performed by a computer search of the *S. aureus* genome for the identified sequence. Alternatively, tryptic peptide fragments of the *S. aureus* genome can be predicted by computer software based on the nucleotide sequence of the genome, and the predicted molecular mass of peptide fragments generated *in silico* compared to the molecular mass of the peptides obtained from each interacting protein eluted from the affinity matrix.

In addition, an oligonucleotide cocktail can be synthesized based on the primary amino acid sequence determined for an interacting *S. aureus* protein fragment. This oligonucleotide cocktail would comprise a mixture of oligonucleotides based on the nucleotide sequences of the primary amino acid of the predicted peptide, but in which all possible codons for a particular amino acid sequence are present in a subset of the oligonucleotide pool. This cocktail can then be used as a degenerate probe set to screen, by hybridization to genomic or cDNA libraries, to isolate the corresponding gene.

Alternatively, antibodies raised to peptides which correspond to an interacting *S. aureus* protein fragment can be used to screen expression libraries (genomic or cDNA) to identify the gene encoding the interacting protein.

Vectors

The invention also provides vectors, preferably expression vectors, harboring the anti-microbial DNA nucleic acid segment of the invention in an expressible form, and cells transformed with the same. Such cells can serve a variety of purposes, such as *in vitro* models for the function of the anti-microbial nucleic acid segment and screening for downstream targets of the anti-microbial nucleic acid segment, as well as expression to provide relatively large quantities of the inhibitory product.

Thus, an expression vector harboring the anti-microbial nucleic acid segment or parts thereof (*Staph A* bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182) can also be used to obtain substantially pure protein. Well-known vectors, such as the pGEX series (available from Pharmacia), can be used to obtain large amounts of the protein which can then be purified by standard biochemical methods based on charge, molecular mass, solubility, or affinity selection of the protein by using gene fusion techniques (such as GST fusion, which permits the purification of the protein of interest on a glutathione column). Other types of purification methods or fusion proteins could also be used as recognized by those skilled in the art.

Likewise, vectors containing bacteriophage 77 ORFs 17, 19, 43, 102, 104, and 182 can be used in methods for identifying targets of the encoded antibacterial ORF product, e.g., as described above, and/or for testing inhibition of homologous bacterial targets or other potential targets in bacterial species other than *Staphylococcus aureus*.

Antibodies

Antibodies, both polyclonal and monoclonal, can be prepared against the protein encoded by a bacteriophage anti-microbial DNA segment of the invention (e.g., *Staph A* bacteriophage 77 ORF 17, 19, 43, 102, 104, or 182) by methods well known in the art. Protein for preparation of such antibodies can be prepared by purification, usually from a recombinant cell expressing the specified ORF or fragment thereof. Those skilled in the art are familiar with methods for preparing polyclonal or monoclonal antibodies (See, e.g., Antibodies: A Laboratory Manual, Harlow and Lane, Cold Spring Harbor Laboratory, CSHL Press, N.Y., 1988).

Such antibodies can be used for a variety of purposes including affinity purification of the protein encoded by the bacteriophage anti-microbial DNA segment, tethering of the protein encoded by the bacteriophage anti-microbial DNA segment to a solid matrix for purposes of identifying interacting host bacterium proteins, and for monitoring of expression of the protein encoded by the bacteriophage anti-microbial DNA segment.

Recombinant Cells

Bacterial cells containing an inducible vector regulating expression of the bacteriophage anti-microbial DNA segment can be used to generate an animal model

system for the study of infection by the host bacterium. The functional activity of the proteins encoded by the bacteriophage anti-microbial DNA segments, whether native or mutated, can be tested in animal *in vitro* or *in vivo* models.

While such cells containing inducible expression vectors is preferred, other
5 recombinant cells containing a recombinant phage 77 ORF 17, 19, 43, 102, 104, or 182 sequence or portion thereof are also provided by the present invention.

Also, a recombinant cell may contain a recombinant sequence encoding at least a portion of a protein which is a target of phage 77 ORF 17, 19, 43, 102, 104, or 182 inhibitory ORF product.

10 In the context of this invention, in connection with nucleic acid sequences, the term "recombinant" refers to nucleic acid sequences which have been placed in a genetic location by intervention using molecular biology techniques, and does not include the relocation of phage sequences during or as a result of phage infection of a bacterium or normal genetic exchange processes such as bacterial conjugation.

15

Derivatization of identified anti-microbials

In cases where the identified anti-microbials above are peptidic compounds, the *in vivo* effectiveness of such compounds may be advantageously enhanced by
20 chemical modification using the natural polypeptide as a starting point and incorporating changes that provide advantages for use, for example, increased stability to proteolytic degradation, reduced antigenicity, improved tissue penetration, and/or improved delivery characteristics.

In addition to active modifications and derivative creations, it can also be
25 useful to provide inactive modifications or derivatives for use as negative controls or introduction of immunologic tolerance. For example, a biologically inactive derivative which has essentially the same epitopes as the corresponding natural antimicrobial can be used to induce immunological tolerance in a patient being treated. The induction of tolerance can then allow uninterrupted treatment with the
30 active anti-microbial to continue for a significantly longer period of time.

Modified anti-microbial polypeptides and derivatives can be produced using a number of different types of modifications to the amino acid chain. Many such methods are known to those skilled in the art. The changes can include, for example, reduction of the size of the molecule, and/or the modification of the amino

acid sequence of the molecule. In addition, a variety of different chemical modifications of the naturally occurring polypeptide can be used, either with or without modifications to the amino acid sequence or size of the molecule. Such chemical modifications can, for example, include the incorporation of modified or non-natural amino acids or non-amino acid moieties during synthesis of the peptide chain, or the post-synthesis modification of incorporated chain moieties.

The oligopeptides of this invention can be synthesized chemically or through an appropriate gene expression system. Synthetic peptides can include both naturally occurring amino acids and laboratory synthesized, modified amino acids.

Also provided herein are functional derivatives of anti-microbial proteins or polypeptides. By "functional derivative" is meant a "chemical derivative," "fragment," "variant," "chimera," or "hybrid" of the polypeptide or protein, which terms are defined below. A functional derivative retains at least a portion of the function of the protein, for example, reactivity with a specific antibody, enzymatic activity or binding activity.

A "chemical derivative" of the complex contains additional chemical moieties not normally a part of the protein or peptide. Such moieties may improve the molecule's solubility, absorption, biological half-life, and the like. The moieties may alternatively decrease the toxicity of the molecule, eliminate or attenuate any undesirable side effect of the molecule, and the like. Moieties capable of mediating such effects are disclosed in Alfonso and Gennaro (1995). Procedures for coupling such moieties to a molecule are well known in the art. Covalent modifications of the protein or peptides are included within the scope of this invention. Such modifications may be introduced into the molecule by reacting targeted amino acid residues of the peptide with an organic derivatizing agent that is capable of reacting with selected side chains or terminal residues, as described below.

Cysteiny l residues most commonly are reacted with alpha-haloacetates (and corresponding amines), such as chloroacetic acid or chloroacetamide, to give carboxymethyl or carboxyamidomethyl derivatives. Cysteiny l residues also are derivatized by reaction with bromotrifluoroacetone, chloroacetyl phosphate, N-alkylmaleimides, 3-nitro-2-pyridyl disulfide, methyl 2-pyridyl disulfide, p-chloro-mercuribenzoate, 2-chloromercuri-4-nitrophenol, or chloro-7-nitrobenzo-2-oxa-1,3-diazole.

Histidyl residues are derivatized by reaction with diethylprocarbonate at pH 5.5-7.0 because this agent is relatively specific for the histidyl side chain. Para-bromophenacyl bromide also is useful; the reaction is preferably performed in 0.1 M sodium cacodylate at pH 6.0.

5 Lysinyl and amino terminal residues are reacted with succinic or other carboxylic acid anhydrides. Derivatization with these agents has the effect of reversing the charge of the lysinyl residues. Other suitable reagents for derivatizing primary amine- containing residues include imidoesters such as methyl
10 trinitrobenzenesulfonic acid; O-methylisourea; 2,4 pentanedione; and transaminase-catalyzed reaction with glyoxylate.

Arginyl residues are modified by reaction with one or several conventional reagents, among them phenylglyoxal, 2,3-butanedione, 1,2-cyclohexanedione, and
15 ninhydrin. Derivatization of arginine residues requires that the reaction be performed in alkaline conditions because of the high pK_a of the guanidine functional group. Furthermore, these reagents may react with the groups of lysine as well as the arginine alpha-amino group.

Tyrosyl residues are well-known targets of modification for introduction of spectral labels by reaction with aromatic diazonium compounds or
20 tetranitromethane. Most commonly, N-acetylimidizol and tetranitromethane are used to form O-acetyl tyrosyl species and 3-nitro derivatives, respectively.

Carboxyl side groups (aspartyl or glutamyl) are selectively modified by reaction carbodiimide ($R'-N-C-N-R'$) such as 1-cyclohexyl-3-(2-morpholinyl(4-ethyl) carbodiimide or 1-ethyl-3-(4-azonia-4,4-dimethylpentyl) carbodiimide.
25 Furthermore, aspartyl and glutamyl residues are converted to asparaginyl and glutaminyl residues by reaction with ammonium ions.

Glutaminyl and asparaginyl residues are frequently deamidated to the corresponding glutamyl and aspartyl residues. Alternatively, these residues are deamidated under mildly acidic conditions. Either form of these residues falls
30 within the scope of this invention.

Derivatization with bifunctional agents is useful, for example, for cross-linking component peptides to each other or the complex to a water-insoluble support matrix or to other macromolecular carriers. Commonly used cross-linking agents include, for example, 1,1-bis (diazoacetyl)-2-phenylethane, glutaraldehyde,

N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), and bifunctional maleimides such as bis-N-maleimido-1,8-octane. Derivatizing agents such as methyl-3-[p-azidophenyl] dithiolpropioimide yield photoactivatable intermediates that are capable of forming crosslinks in the presence of light. Alternatively, reactive water-insoluble matrices such as cyanogen bromide-activated carbohydrates and the reactive substrates described in U.S. Patent Nos. 3,969,287; 3,691,016; 4,195,128; 4,247,642; 4,229,537; and 4,330,440 are employed for protein immobilization.

Other modifications include hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the alpha-amino groups of lysine, arginine, and histidine side chains (Creighton, T.E., *Proteins: Structure and Molecular Properties*, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)), acetylation of the N-terminal amine, and, in some instances, amidation of the C-terminal carboxyl groups.

Such derivatized moieties may improve the stability, solubility, absorption, biological half-life, and the like. The moieties may alternatively eliminate or attenuate any undesirable side effect of the protein complex. Moieties capable of mediating such effects are disclosed, for example, in Alfonso and Gennaro (1995).

The term "fragment" is used to indicate a polypeptide derived from the amino acid sequence of the protein or polypeptide having a length less than the full-length polypeptide from which it has been derived. Such a fragment may, for example, be produced by proteolytic cleavage of the full-length protein. Preferably, the fragment is obtained recombinantly by appropriately modifying the DNA sequence encoding the proteins to delete one or more amino acids at one or more sites of the C-terminus, N-terminus, and/or within the native sequence.

Another functional derivative intended to be within the scope of the present invention is a "variant" polypeptide which either lacks one or more amino acids or contains additional or substituted amino acids relative to the native polypeptide. The variant may be derived from a naturally occurring polypeptide by appropriately modifying the protein DNA coding sequence to add, remove, and/or to modify codons for one or more amino acids at one or more sites of the C-terminus, N-terminus, and/or within the native sequence.

A functional derivative of a protein or polypeptide with deleted, inserted and/or substituted amino acid residues may be prepared using standard techniques well-known to those of ordinary skill in the art. For example, the modified components of the functional derivatives may be produced using site-directed
5 mutagenesis techniques (as exemplified by Adelman et al., 1983, *DNA* 2:183; Sambrook et al., 1989) wherein nucleotides in the DNA coding sequence are modified such that a modified coding sequence is produced, and thereafter expressing this recombinant DNA in a prokaryotic or eukaryotic host cell, using techniques such as those described above. Alternatively, components of functional
10 derivatives of complexes with amino acid deletions, insertions and/or substitutions may be conveniently prepared by direct chemical synthesis, using methods well-known in the art.

Insofar as other anti-microbial inhibitor compounds identified by the invention described herein may not be peptidal in nature, other chemical techniques
15 exist to allow their suitable modification, as well, and according the desirable principles discussed above.

Administration and Pharmaceutical Compositions

20

For the therapeutic and prophylactic treatment of infection, the preferred method of preparation or administration of anti-microbial compounds will generally vary depending on the precise identity and nature of the anti-microbial being delivered. Thus, those skilled in the art will understand that administration methods
25 known in the art will also be appropriate for the compounds of this invention. Pharmaceutical compositions are prepared, as understood by those skilled in the art, to be appropriate for therapeutic use. Thus, generally the components and composition are prepared to be sterile and free of components or contaminants which would pose an unacceptable risk to a patient. For compositions to be
30 administered internally is is generally important that the composition be pyrogen free, for example.

The particularly desired anti-microbial can be administered to a patient either by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s). In treating an infection, a therapeutically effective amount of an
35 agent or agents is administered. A therapeutically effective dose refers to that

amount of the compound that results in amelioration of one or more symptoms of bacterial infection and/or a prolongation of patient survival or patient comfort.

Toxicity, therapeutic and prophylactic efficacy of anti-microbials can be determined by standard pharmaceutical procedures in cell cultures and/or experimental organisms such as animals, *e.g.*, for determining the LD₅₀ (the dose lethal to 50% of the population) and the ED₅₀ (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD₅₀/ED₅₀. Compounds which exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED₅₀ with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized.

For any compound identified and used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. Such information can be used to more accurately determine useful doses in organisms such as plants and animals, preferably mammals, and most preferably humans. Levels in plasma may be measured, for example, by HPLC or other means appropriate for detection of the particular compound.

The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition (see *e.g.* Fingl et. al., in The Pharmacological Basis of Therapeutics, 1975, Ch. 1 p.1).

It should be noted that the attending physician would know how and when to terminate, interrupt, or adjust administration due to toxicity, organ dysfunction, or other systemic malady. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administered dose in the management of the disorder of interest will vary with the severity of the condition to be treated and the route of administration. The severity of the condition may, for example, be evaluated, in part, by standard prognostic evaluation methods. Further, the dose and perhaps dose frequency, will also vary according to the age, body weight, and response of the individual patient. A program comparable to that discussed above also may be used in veterinary or phyto medicine.

Depending on the specific infection target being treated and the method selected, such agents may be formulated and administered systemically or locally, i.e., topically. Techniques for formulation and administration may be found in Alfonso and Gennaro (1995). Suitable routes may include, for example, oral, rectal, 5 transdermal, vaginal, transmucosal, intestinal, parenteral, intramuscular, subcutaneous, or intramedullary injections, as well as intrathecal, intravenous, or intraperitoneal injections.

For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, 10 Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

Use of pharmaceutically acceptable carriers to formulate identified anti-microbials of the present invention into dosages suitable for systemic administration 15 is within the scope of the invention. With proper choice of carrier and suitable manufacturing practice, the compositions of the present invention, in particular those formulated as solutions, may be administered parenterally, such as by intravenous injection. Appropriate compounds can be formulated readily using pharmaceutically acceptable carriers well known in the art into dosages suitable for oral 20 administration. Such carriers enable the compounds of the invention to be formulated as tablets, pills, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

Agents intended to be administered intracellularly may be administered using techniques well known to those of ordinary skill in the art. For example, such agents 25 may be encapsulated into liposomes, then administered as described above. Liposomes are spherical lipid bilayers with aqueous interiors. All molecules present in an aqueous solution at the time of liposome formation are incorporated into the aqueous interior. The liposomal contents are both protected from the external microenvironment and, because liposomes fuse with cell membranes, are efficiently 30 delivered into the cell cytoplasm. Additionally, due to their hydrophobicity, small organic molecules may be directly administered intracellularly.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to

achieve the intended purpose. Determination of the effective amounts is well within the capability of those skilled in the art.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. The preparations formulated for oral administration may be in the form of tablets, dragees, capsules, or solutions, including those formulated for delayed release or only to be released when the pharmaceutical reaches the small or large intestine.

The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levitating, emulsifying, encapsulating, entrapping or lyophilizing processes.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active anti-microbial compounds in water-soluble form. Alternatively, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical preparations for oral use can be obtained by combining the active compounds with solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures.

- 5 Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active
10 ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

- 15 The above methodologies may be employed either actively or prophylactically against an infection of interest.

To identify DNA segments of *Staph A* bacteriophage 77 capable of acting as anti-microbial agents, a strategy described in a existing provisional patent was
20 employed (U.S. Provisional Application No. 60/110,992, and filed Dec. 3, 1998). In essence, the procedure involved sequence characterization of the bacteriophage, identification of protein coding regions (open reading frames or ORFs), subcloning of all ORFs into an appropriate inducible expression vector, transfer of the ORF subclones into *Staph. A*, followed by induction of ORF expression and assessment of
25 effect on growth. We employed discovery steps as described in the Examples.

Example I. Growth of *Staph A* bacteriophage 77 and purification of genomic DNA.

The *Staphylococcus aureus* propagating strain (PS 77; ATCC #27699) was
30 used as a host to propagate its respective phage 77 (ATCC # 27699-B1). Two rounds of plaque purification of phage 77 were performed on soft agar essentially as described in Sambrook et al (1989). Briefly, the PS 77 strain was grown overnight at 37°C in Nutrient broth [NB: 0.3% Bacto beef extract, 0.5% Bacto peptone (Difco Laboratories) and 0.5% NaCl (w/v)]. The culture was then diluted 20x in NB and

incubated at 37°C until the $OD_{540} = .2$ (early log phase) with constant agitation. In order to obtain single plaques, phage 77 was subjected to 10-fold serial dilutions using phage buffer (1 mM $MgSO_4$, 5 mM $MgCl_2$, 80 mM NaCl and 0.1% Gelatin (w/v)) and 10 μ l of each dilution was used to infect 0.5 ml of the cell suspension in the presence of 400 μ g/ml $CaCl_2$. After incubation of 15 min at room temperature (RT), 2 ml of melted soft agar kept at 45°C (NB supplemented with 0.6% agar) was added to the mixture and poured onto the surface of 100 mm nutrient agar plates (0.3% Bacto Beef extract, 0.5% Bacto peptone, 0.5% NaCl and 1.5% Bacto agar (w/v)). After overnight incubation at 30°C, a single plaque was isolated, resuspended in 1 ml of phage buffer by end over end rotation for 2 hrs at 20°C, and the phage suspension was diluted and used for a second infection as described above. After overnight incubation at 30°C, a single plaque was isolated and used as a stock.

The propagation procedure for bacteriophage 77 was modified from the agar layer method of Swanst rm and Adams (1951). Briefly, the PS 77 strain was grown to stationary phase overnight at 37°C in Nutrient broth. The culture was then diluted twenty-fold in NB and incubated at 37°C until the $OD_{540} = .2$. The suspension (15×10^7 Bacteria) was then mixed with 15×10^5 plaque forming units (pfu) to give a ratio of 100-bacteria/phage particle in the presence of 400 μ g/ml of $CaCl_2$. After incubation for 15 min at 20°C, 7.5 ml of melted soft agar (NB plus 0.6% agar) were added to the mixture and poured onto the surface of 150 mm nutrient agar plates and incubated 16 hrs at 30°C. To collect the phage plate lysate, 20 ml of NB were added to each plate and the soft agar layer was collected by scrapping off with a clean microscope slide followed by shaking of the agar suspension for 5 min to break up the agar. The mixture was then centrifuged for 10 min at 4,000 RPM (2,830xg) in a JA-10 rotor (Beckman) and the supernatant fluid (lysate) was collected and subjected to a treatment with 10 μ g /ml of DNase I and RNase A for 30 min at 37°C. To precipitate the phage particles, the phage suspension was adjusted to 10% (w/v) PEG 8000 and 0.5 M of NaCl followed by incubation at 4°C for 16 hrs. The phage was recovered by centrifugation at 4,000 rpm (3,500xg) for 20 min at 4°C on a GS-6R table top centrifuge (Beckman). The pellet was resuspended with 2 ml of phage buffer (1 mM $MgSO_4$, 5 mM $MgCl_2$, 80 mM NaCl and 0.1% Gelatin). The phage suspension was extracted with 1 volume of chloroform and further purified by centrifugation on a cesium chloride step gradient as described in Sambrook et al.

(1989), using a TLS 55 rotor centrifuged in an Optima TLX ultracentrifuge (Beckman) for 2 h at 28,000 rpm (67,000xg) at 4°C. Banded phage was collected and ultracentrifuged again on an isopycnic cesium chloride gradient (1.45 g/ml) at 40,000 rpm (64,000xg) for 24 h at 4°C using a TLV rotor (Beckman). The phage
5 was harvested and dialyzed for 4 h at room temperature against 4 L of dialysis buffer consisting of 10 mM NaCl, 50 mM Tris-HCl [pH 8] and 10 mM MgCl₂. Phage DNA was prepared from the phage suspension by adding 20 mM EDTA, 50 mg/ml Proteinase K and 0.5% SDS and incubating for 1 h at 65°C, followed by successive extractions with 1 volume of phenol, 1 volume of phenol-chloroform and
10 1 volume of chloroform. The DNA was then dialyzed overnight at 4°C against 4 L of TE (10 mM Tris pH 8.0, 1mM EDTA).

Example II. DNA sequencing of Bacteriophage 77 genome

Four micrograms of phage DNA was diluted in 200 µl of TE (10 mM Tris, [pH 8.0], 1 mM EDTA) in a 1.5 ml eppendorf tube and sonication was performed (550 Sonic Dismembrator™, Fisher Scientific). Samples were sonicated under an amplitude of 3 µm with bursts of 5 s spaced by 15 s cooling in ice/water for 3 to 4 cycles. The sonicated DNA was then size fractionated by electrophoresis on 1% agarose gels utilizing TAE (1 x TAE is: 40 mM Tris-acetate, 1 mM EDTA [pH 8.0])
20 as the running buffer. Fractions ranging from 1 to 2 kbp were excised from the agarose gel and purified using a commercial DNA extraction system according to the instructions of the manufacturer (Qiagen), with a final elution of 50 µl of 1 mM Tris (pH 8.5).

The ends of the sonicated DNA fragments were repaired with a combination
25 of T4 DNA polymerase and the Klenow fragment of E. coli DNA polymerase I, as follows. Reactions were performed in a reaction mixture (final volume, 100 µl) containing sonicated phage DNA, 10 mM Tris-HCl [pH 8.0], 50 mM NaCl, 10 mM MgCl₂, 1 mM DTT, 50 µg/ml BSA, 100 µM of each dNTP and 15 units of T4 DNA polymerase (New England Biolabs) for 20 min at 12°C followed by addition of 12.5
30 units of Klenow large fragment (New England Biolabs) for 15 min at room temperature. The reaction was stopped by two phenol/chloroform extractions and the DNA was precipitated with ethanol and the final DNA pellet was resuspended in 20 µl of H₂O.

Blunt-ended DNA fragments were cloned by ligation directly into the *Hinc* II site of pKSII+ vector (New England Biolabs) dephosphorylated by treatment with calf intestinal alkaline phosphatase (New England Biolabs)-treated pKS II+ vector (Stratagene). A typical ligation reaction contained 100 ng of vector DNA, 2 to 5 μ l of repaired sonicated phage DNA (50-100 ng) in a final volume of 20 μ l containing 800 units of T4 DNA ligase (New England Biolabs) and was incubated overnight at 16°C. Transformation and selection of bacterial clones containing recombinant plasmids was performed in *E. coli* DH10 β according to standard procedures (Sambrook et al., 1989).

Recombinant clones were picked from agar plates into 96-well plates containing 100 μ l LB and 100 μ g/ml ampicillin and incubated at 37°C. The presence of phage DNA insert was confirmed by PCR amplification using T3 and T7 primers flanking the *Hinc* II cloning site of the pKS II+ vector. PCR amplification of foreign insert was performed in a 15 μ l reaction volume containing 10 mM Tris (pH 8.3), 50 mM KCl, 1.5 mM MgCl₂, 0.02% gelatin, 1 μ M primer, 187.5 μ M each dNTP, and 0.75 units *Taq* polymerase (BRL). The thermocycling parameters were as follows: 2 min initial denaturation at 94°C for 2 min, followed by 20 cycles of 30 sec denaturation at 94°C, 30 sec annealing at 57°C, and 2 min extension at 72°C, followed by a single extension step at 72°C for 10 min. Clones with insert sizes of 1 to 2 kbp were selected and plasmid DNA was prepared from the selected clones using QIAprep™ spin miniprep kit (Qiagen).

The nucleotide sequence of the extremities of each recombinant clone was determined using an ABI 377-36 automated sequencer with two types of chemistry: ABI prism Big Dye™ primer or ABI prism Big Dye™ terminator cycle sequencing ready reaction kit (Applied Biosystems). To ensure co-linearity of the sequence data and the genome, all regions of phage genome were sequenced at least once from both directions on two separate clones. In areas that this criteria was not initially met, a sequencing primer was selected and phage DNA was used directly as sequencing template employing ABI prism Big Dye™ terminator cycle sequencing ready reaction kit.

Example III. Bioinformatic management of primary nucleotide sequence.

Sequence contigs were assembled using Sequencher™ 3.1 software (GeneCodes). To close contig gaps, sequencing primers were selected near the edge of the contigs. Phage DNA was used directly as sequencing template employing ABI prism BIG DYE™ terminator cycle sequencing ready reaction kit. The complete sequence of bacteriophage 77 is shown in Table 1.

A software program was developed and used on the assembled sequence of bacteriophage 77 to identify all putative ORFs larger than 33 codons. Other ORF identification software can also be utilized, preferably programs which allow alternative start codons. The software scans the primary nucleotide sequence starting at nucleotide #1 for an appropriate start codon. Three possible selections can be made for defining the nature of the start codon; I) selection of ATG, II) selection of ATG or GTG, and III) selection of either ATG, GTG, TTG, CTG, ATT, ATC, and ATA. This latter initiation codon set corresponds to the one reported by the NCBI (<http://www.ncbi.nlm.nih.gov/htbin-post/Taxonomy/wprintgc?mode=c>) for the bacterial genetic code.

When an appropriate start codon is encountered, a counting mechanism is employed to count the number of codons (groups of three nucleotides) between this start codon and the next stop codon downstream of it. If a threshold value of 33 is reached, or exceeded, then the sequence encompassed by these two codons (start and stop codons) is defined as an ORF. This procedure is repeated, each time starting at the next nucleotide following the previous stop codon found, in order to identify all the other putative ORFs. The scan is performed on all three reading frames of both DNA strands of the phage sequence.

Sequence homology (BLAST) searches for each ORF are then carried out using an implementation of BLAST programs, although any of a variety of different sequence comparison and matching programs can be utilized as known to those skilled in the art. Downloaded public databases used for sequence analysis include:

- i) non-redundant GenBank (<ftp://ncbi.nlm.nih.gov/blast/db/nr.Z>),
- ii) Swissprot (<ftp://ncbi.nlm.nih.gov/blast/db/swissprot.Z>);
- iii) vector (<ftp://ncbi.nlm.nih.gov/blast/db/vector.Z>);
- iv) pdbaa databases (<ftp://ncbi.nlm.nih.gov/blast/db/pdbaa.Z>);
- v) staphylococcus aureus NCTC 8325 (<ftp://ftp.genome.ou.edu/pub/staph/staph-1k.fa>);
- vi) streptococcus pyogenes (<ftp://ftp.genome.ou.edu/pub/strep/strep-1k.fa>);

vii) streptococcus pneumoniae

(ftp://ftp.tigr.org/pub/data/s_pneumoniae/gsp.contigs.112197.Z);

viii) mycobacterium tuberculosis CSU#9

(ftp://ftp.tigr.org/pub/data/m_tuberculosis/TB_091097.Z) and ix)

5 pseudomonas aeruginosa

(http://www.genome.washington.edu/pseudo/data.html).

The results of the homology searches performed on the ORFs is shown in Table 4.

10 **Example IV. Subcloning of Bacteriophage 77 ORFs into a Staph A inducible expression system.**

The shuttle vector pT0021, in which the firefly luciferase (*lucFF*) expression is controlled by the *ars* (arsenite) promoter/operator (Tauriainen et al., 1997), was modified in the following fashion. Two oligonucleotides corresponding to a short
15 antigenic peptide derived from the hemagglutinin protein of influenza virus (HA epitope tag) were synthesized (Field et al., 1988). The sense strand HA tag sequence (with *Bam*HI, *Sal*I and *Hind*III cloning sites) is:

5'-gatcccggtcgaccaagcttTACCCATACGACGTCCTCCAGACTACGCCAGCTGA-3'

(where upper case letters denote the nucleotide sequence of the HA tag); the

20 antisense strand HA tag sequence (with a *Hind*III cloning site) is:

5'-agctTCAGCTGGCGTAGTCTGGGACGTCGTATGGGTAAagcttggtcgaccgg-3'

(where upper case letters denote the sequence of the HA tag). The two HA tag oligonucleotides were annealed and ligated into pT0021 vector which had been digested with *Bam*HI and *Hind*III. This manipulation resulted in replacement of the
25 *lucFF* gene by the HA tag. This modified shuttle vector containing the *arsenite* inducible promoter, the *arsR* gene, and HA tag was named pTHA. A diagram outlining our modification of pT0021 to generate pTHA is shown in Fig. 1.

Each ORF, encoded by Bacteriophage 77, larger than 33 amino acids and having a Shine-Dalgarno sequence upstream of the initiation codon was selected for
30 functional analysis for bacterial inhibition. In total, 98 ORFs were selected and screened as detailed below. A list of these is presented in Table 5. Each individual ORF, from initiation codon to last codon (excluding the stop codon), was amplified from phage genomic DNA using the polymerase chain reaction (PCR). For PCR amplification of ORFs, each sense strand primer targets the initiation codon and is

preceded by a *Bam*HI restriction site (^{5'}cgggatcc^{3'}) and each antisense oligonucleotide targets the pentultimate codon (the one before the stop codon) of the ORF and is preceded by a *Sal* I restriction site (^{5'}gcgtcgaccg^{3'}). The PCR product of each ORF was gel purified and digested with *Bam*HI and *Sal*I. The digested PCR product was then gel purified using the Qiagen kit as described, ligated into *Bam*HI and *Sal*I digested pTHA vector, and used to transform *E. coli* bacterial strain DH10β (as described above). As a result of this manipulation, the HA tag is set inframe with the ORF and is positioned at the carboxy terminus of each ORF (pTHA/ORF clones). Recombinant pTHA/ORF clones were picked and their insert sizes were confirmed by PCR analysis using primers flanking the cloning site. The names and sequences of the primers that were used for the PCR amplification were: HAF: 5'TATTATCCAAAACCTTGAACA^{3'}; HAR: 5'CGGTGGTATATCCAGTGATT^{3'}. The sequence integrity of cloned ORFs was verified directly by DNA sequencing using primers HAF and HAR. In cases where verification of ORF sequence could not be achieved by one pass with the sequencing primers, additional internal primers were selected and used for sequencing.

Staphylococcus aureus strain RN4220 (Kreiswirth et al., 1983) was used as a recipient for the expression of recombinant plasmids. Electroporation was performed essentially as previously described (Schenk and Laddaga, 1992). Selection of recombinant clones was performed on Luria-Broth agar (LB-agar) plates containing 30 µg/ml of kanamycin.

For each ORF introduced in the pTHA plasmid, 3 independent transformants were isolated and used to individually inoculate cultures in 5 ml of TSB containing 30µg/ml kanamycin, followed by growth to saturation (16 hrs at 30°C). An aliquot of this stationary phase culture was used to generate a frozen glycerol stock of the transformant (stored at - 80°C). The remaining culture was used for plasmid DNA extraction. Bacterial cells were harvested by centrifugation at 3000 x g at 22°C for 5 min. The pellet was resuspended in 200 µl 25% sucrose containing 25U/ml of lysostaphin and incubated for 15 min at 37°C. Then, 400µl of alkaline SDS solution (3% SDS, 0.2N NaOH) were added, well mixed and incubated for 7 min at room temperature. After the alkaline SDS treatment, 300µl of ice-cold 3M sodium acetate pH 4.8 were added, and the mix is immediately spun at 13000g for 15 min at room temperature. The supernatant was transferred to a new 1.5 ml conical centrifuge tube

and 650µl of isopropanol (stored at room temperature) were added. The mix was then centrifuged at 13,000 x g for 5 min. The supernatant fluid was discarded, the pellet washed with 70% ethanol, and resuspended in 320 µl sterile distilled water.

The presence of individual phage 77 ORF DNA inserts in the plasmid was verified by PCR amplification using 1.5 µl transformant miniprep DNA in a PCR with primers flanking the cloning site of ORF in pTHA vector (HAF and HAR). The composition of the PCR reaction and the cycling parameters are identical to those employed for library screening described above.

10 **Example V. Functional assay for bacterial inhibitory activity of bacteriophage 77 ORFs.**

The anti-microbial activity of individual phage 77 ORFs was monitored by two growth inhibitory assays, one on solid agar medium, the other in liquid medium. In general, *Staphylococcus* bacteria transformed with expression plasmids containing individual ORFs were grown in normal TSA medium and stored in 19% glycerol. At pre-determined times, arsenite was added to the culture to induce transcription of the phage 77 ORFs cloned immediately downstream from an arsenite-inducible promoter in the pTHA expression plasmid.

The effect of ORF induction on bacterial growth characteristics was then monitored and quantitated. The growth inhibition assay on solid medium was performed by streaking pTHA/ORF containing *S. aureus* transformant onto LB-Kn and TSA-Kn plates containing increasing concentrations of sodium arsenite (0; 2.5; 5; and 7.5 µM). Arsenite is used to induce the expression of cloned DNA in pTHA vector. In parallel, 3 µl of 1/10 and 1/100 dilutions of the frozen cultures of the pTHA/ORF transformants were spotted as single drops onto LB-Kn and TSA-Kn plates containing increasing concentration of sodium arsenite (0; 2.5; 5; and 7.5 µM). The plates were then incubated 16 hrs at 37°C, and the effect of arsenite-induced ORF expression on bacterial growth was monitored and quantitated by comparing the extent to that seen in control plates. As positive controls for growth inhibition, the *holin/lysin* genes of the *Staphylococcus aureus* phage Twort (Loessner et al., 1998) was subcloned into the pTHA *ars* inducible vector and used.

For the growth inhibition assay in liquid medium, stationary phase cultures were prepared by inoculating 2.5ml TSB-Kn with frozen *S. aureus* RN4220

transformants containing phage 77 ORFs cloned in pTHA vector followed by incubation for 16 hrs at 37°C. These cultures were then diluted 1/100 in the same medium, and the bacteria were allowed to grow for 2 hrs at 37°C to reach early log phase. 150 µl of such culture were then mixed with 2.35 ml TSB-Kn medium with
5 or without arsenite (the final concentration of arsenite in the medium was 0 or 5 µM arsenite). After 3.5 hrs incubation at 37°C with shaking at 250 rpm, 100 µl of bacterial culture was removed from each tube for OD₅₆₅ measurement. Serial ten-fold dilutions of the culture in buffered saline solution (0.85% NaCl) were then spotted onto TSB-Kn plates. The plates were incubated at 37°C 16 hrs and the
10 number of surviving colonies counted the following day. The growth inhibitory property of individual ORFs was then quantitated by comparing CFU numbers under normal or arsenite-induction conditions. Inhibition results are shown in Figures 5 and 5.

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10

All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

15

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The specific methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other

20

uses will occur to those skilled in the art which are encompassed within the spirit of the invention are defined by the scope of the claims.

25

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. For example, those skilled in the art will recognize that the invention may suitably be practiced using a variety of different expression vectors and sequencing methods within the general descriptions provided.

30

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising," "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is not intention that in the use of such terms and expressions of excluding any equivalents

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of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus,

it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope
5 of this invention as defined by the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group. For
10 example, if there are alternatives A, B, and C, all of the following possibilities are included: A separately, B separately, C separately, A and B, A and C, B and C, and A and B and C.

Thus, additional embodiments are within the scope of the invention and within the following claims.

CLAIMS

1. A method for identifying a target for antibacterial agents, comprising determining the bacterial target of a product of a bacteriophage 77 open reading frame selected from the group consisting of open reading frames 17, 19, 43, 102, 104, and 182.
2. The method of claim 1, wherein said determining comprises identifying at least one bacterial protein which binds to said product or a fragment thereof.
3. The method of claim 1, wherein said determining comprises identifying at least one protein:protein interaction using a genetic screen.
4. The method of claim 1, wherein said determining comprises a co-immunoprecipitation assay or a protein-protein crosslinking assay.
5. The method of claim 1, wherein said determining comprises identifying a bacterial coding sequence which protects a bacterium against said bacteriophage inhibitor when expressed at high levels in said bacterium.
6. The method of claim 1, wherein said determining further comprises identifying a bacterial nucleic acid sequence encoding a polypeptide target of said bacteriophage inhibitor protein.
7. The method of claim 1, further comprising determining the cellular or biochemical function or both of said inhibitor protein.
8. The method of claim 1, wherein said identifying the bacterial target comprises identifying a phage-specific site of action.
9. An isolated, purified, or enriched nucleic acid sequence at least 15 nucleotides in length, wherein said sequence corresponds to at least a portion of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 sequence.
10. The nucleic acid sequence of claim 9, wherein said nucleic acid sequence encodes a polypeptide which provides a bacteria-inhibiting function.

11. An isolated, purified, or enriched polypeptide comprising at least a portion of a protein normally encoded by *Staphylococcus aureus* bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182, wherein said portion is at least 5 amino acid residues in length.
12. A recombinant vector comprising a nucleic acid sequence at least 24 nucleotides in length corresponding to a portion of bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182.
13. A recombinant cell comprising a vector, wherein said vector comprises a nucleic acid sequence at least 24 nucleotides in length corresponding to at least a portion of bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182.
14. The cell of claim 13, wherein said vector is an expression vector and expression of said ORF is inducible.
15. A method for identifying an antibacterial agent, comprising identifying an active portion of a product of a bacteria-inhibiting ORF of a bacteriophage.
16. A method for identifying a compound active on a bacterial target protein of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product, comprising the step of
- contacting said bacterial target protein with a test compound; and
- determining whether said compound binds to or reduces the level of activity of said target protein,
- wherein binding of said compound with said target protein or a reduction of the level of activity of said protein is indicative that said compound is active on said target and wherein said target is uncharacterized.
17. The method of claim 16, wherein said contacting is carried out *in vitro*.
18. The method of claim 16, wherein said contacting is carried out *in vivo* in a cell.
19. The method of claim 70, wherein said compound is selected from the group consisting of a small molecule a peptidomimetic compound, or a fragment or derivative of a bacteriophage inhibitor protein.

20. A method of screening for potential antibacterial agents, comprising the step of determining whether any of a plurality of compounds is active on a target of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product, wherein said target is naturally produced by a pathogenic bacterium.

5

21. A method for inhibiting a bacterium, comprising the step of; contacting said bacterium with a compound active on a target of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product, wherein said target or the target site is uncharacterized.

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22. The method of claim 21, wherein said contacting is performed *in vitro*.

23. The method of claim 21, wherein said contacting is performed *in vivo* in an animal or a plant.

15

24. A method for treating a bacterial infection in an animal suffering from an infection, comprising administering to said animal a therapeutically effective amount of compound active on a target of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product in a bacterium involved in said infection,

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wherein said target is an uncharacterized target or the compound is active at an uncharacterized target site.

25

25. The method of claim 24, wherein said compound is selected from the group consisting of a small molecule, a peptidomimetic compound, and a fragment or derivative of a bacteriophage inhibitor protein.

30

26. A method for prophylactically treating an animal at risk of an infection, comprising administering to said animal a prophylactically effective amount of a compound active on a target of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product,

wherein said target is an uncharacterized target or the site of action of said compound is an uncharacterized target site.

35

27. The method of claim 26, wherein said compound is selected from the group consisting of a small molecule, a peptidomimetic compound, and a fragment or derivative of a bacteriophage inhibitor protein.

28. An antibacterial agent active on a target of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product, wherein said target is an uncharacterized target or said agent is active at a phage-specific site on said target.

5 29. The agent of claim 28, wherein said agent is selected from the group consisting of a pepetidomimetic of a bacteriophage inhibitor polypeptide a small molecule, or a fragment or derivative of a bacteriophage inhibitor polypeptide.

30. The agent of claim 28, wherein said agent is a small molecule.

10

31. A method of making an antibacterial agent, comprising the steps of:

a) identifying a target of a bacteriophage 77 open reading frame 17, 19, 43, 102, 104, or 182 product;

15 b) screening a plurality of test compounds to identify a compound active on said target; and

c) synthesizing said compound in an amount sufficient to provide a therapeutic effect when administered to an organism infected by a bacterium naturally producing said target.

20 32. The method of claim 31, wherein said compound is selected from the group consisting of a small molecule, a peptidomimetic compound, and a fragment or derivative of a bacteriophage inhibitor protein.

ABSTRACT

The disclosure concerns particular bacteriophage open reading frame, and portions and products of those open reading frames which have antimicrobial activity. Methods of using such products are also described.

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SD-110719.1

Fig. 1A

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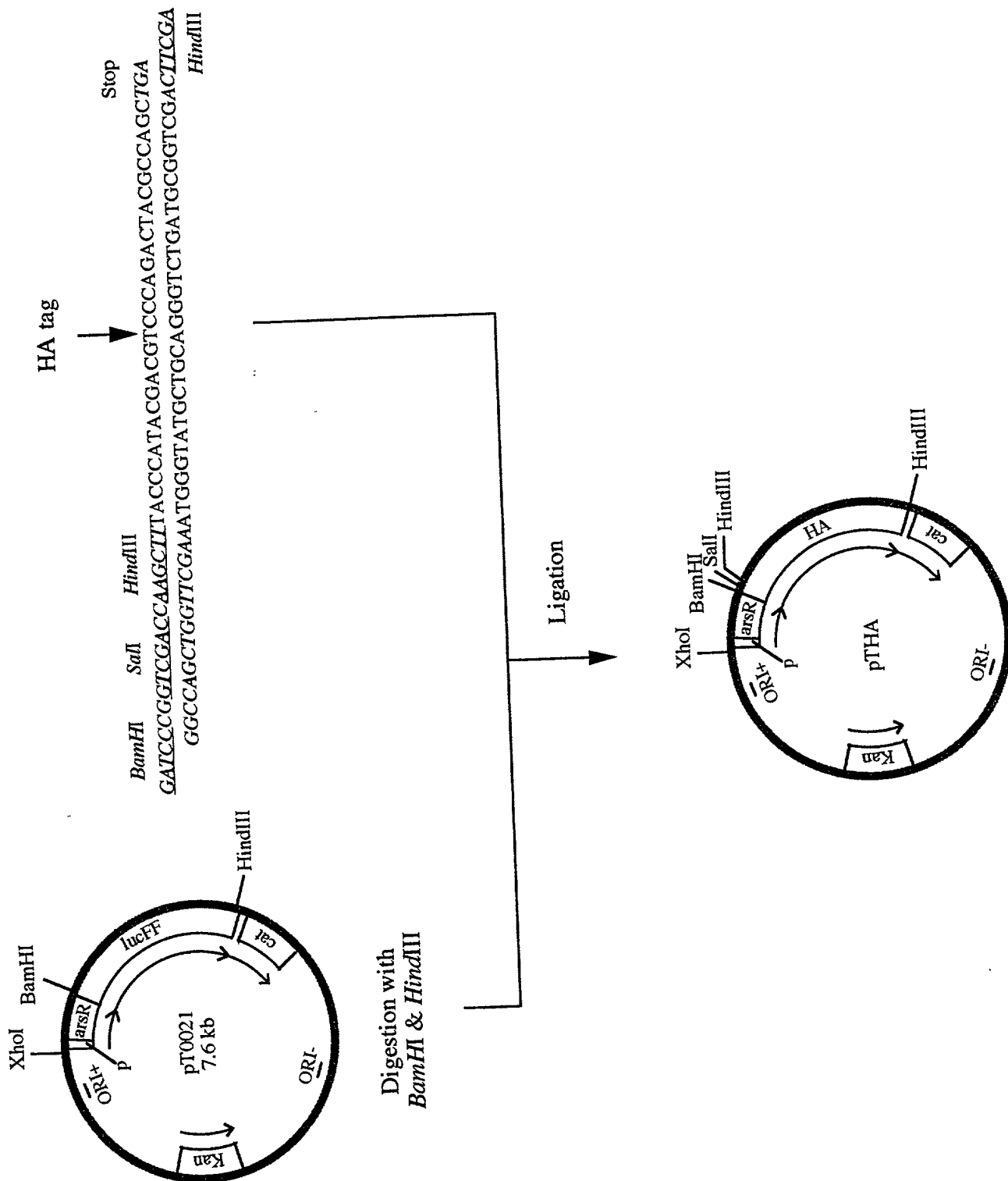
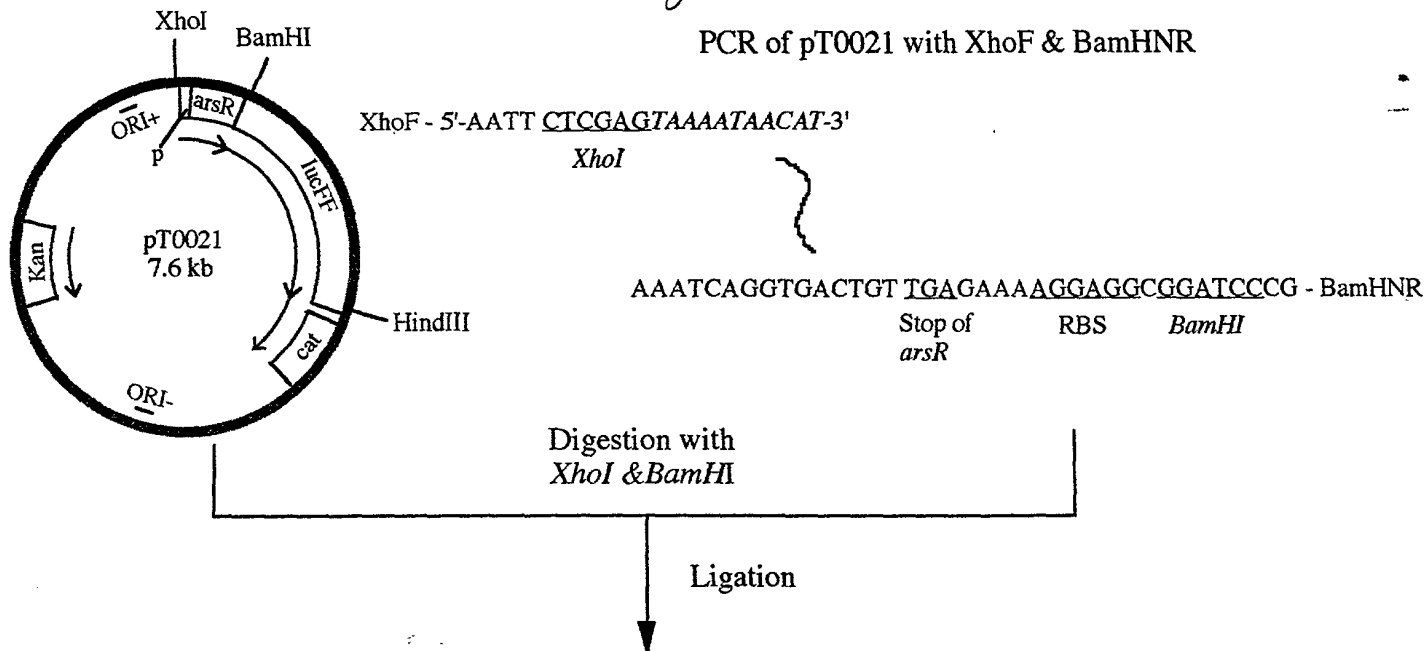
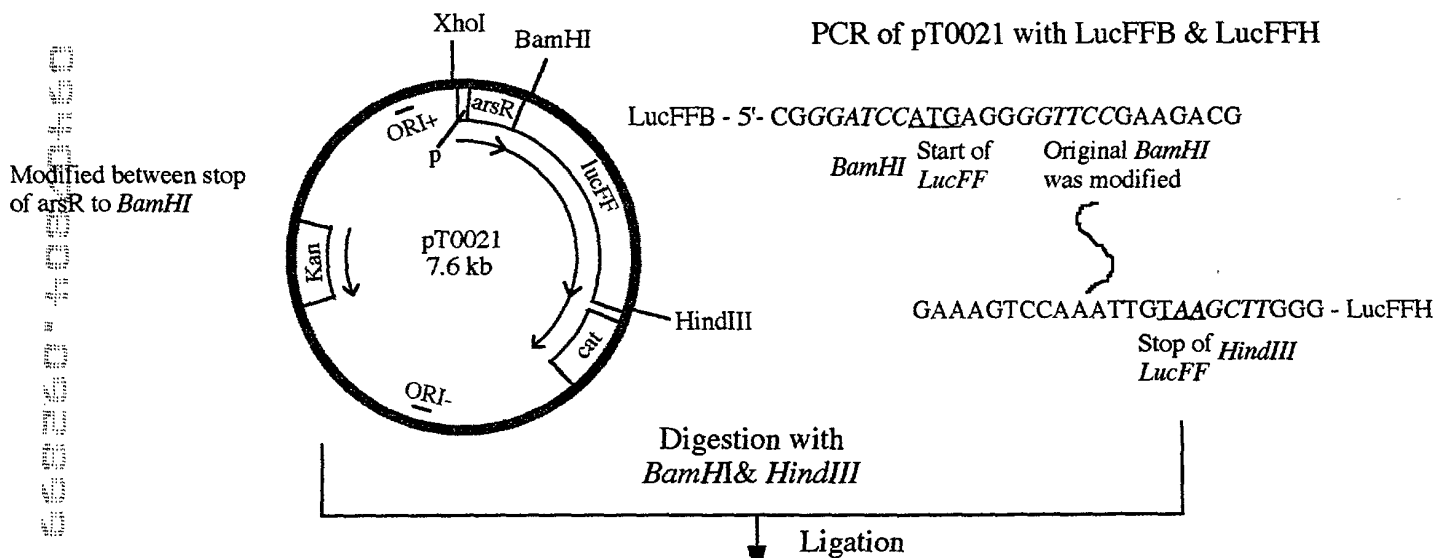


Fig. 1B

PCR of pT0021 with XhoF & BamHNR



PCR of pT0021 with LucFFB & LucFFH



Modified in the vicinity of *BamHI*

Cloning site for ORFs: *BamHI* & *HindIII*

No additional codons in the induced protein

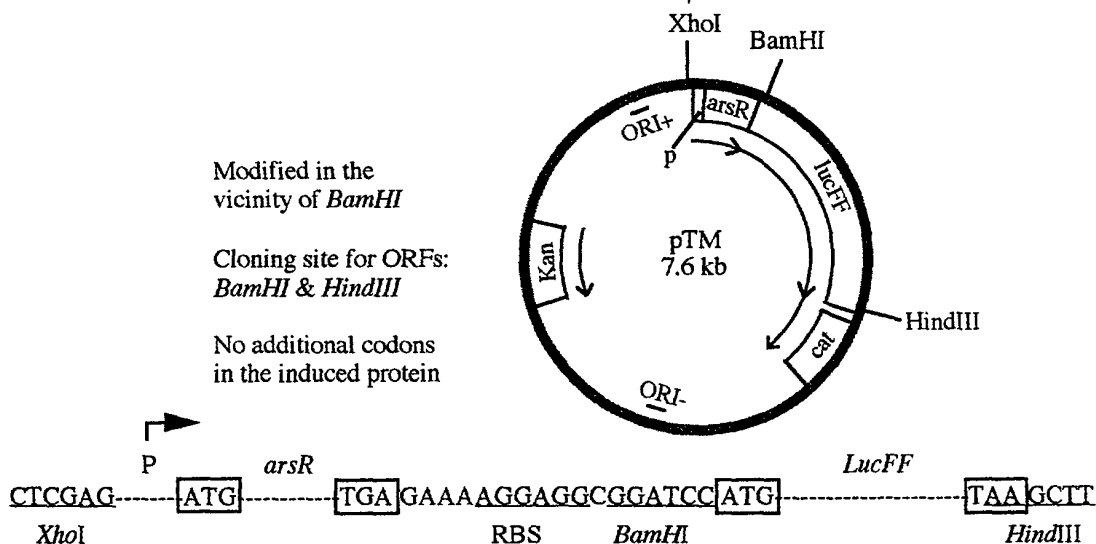


Fig. 2

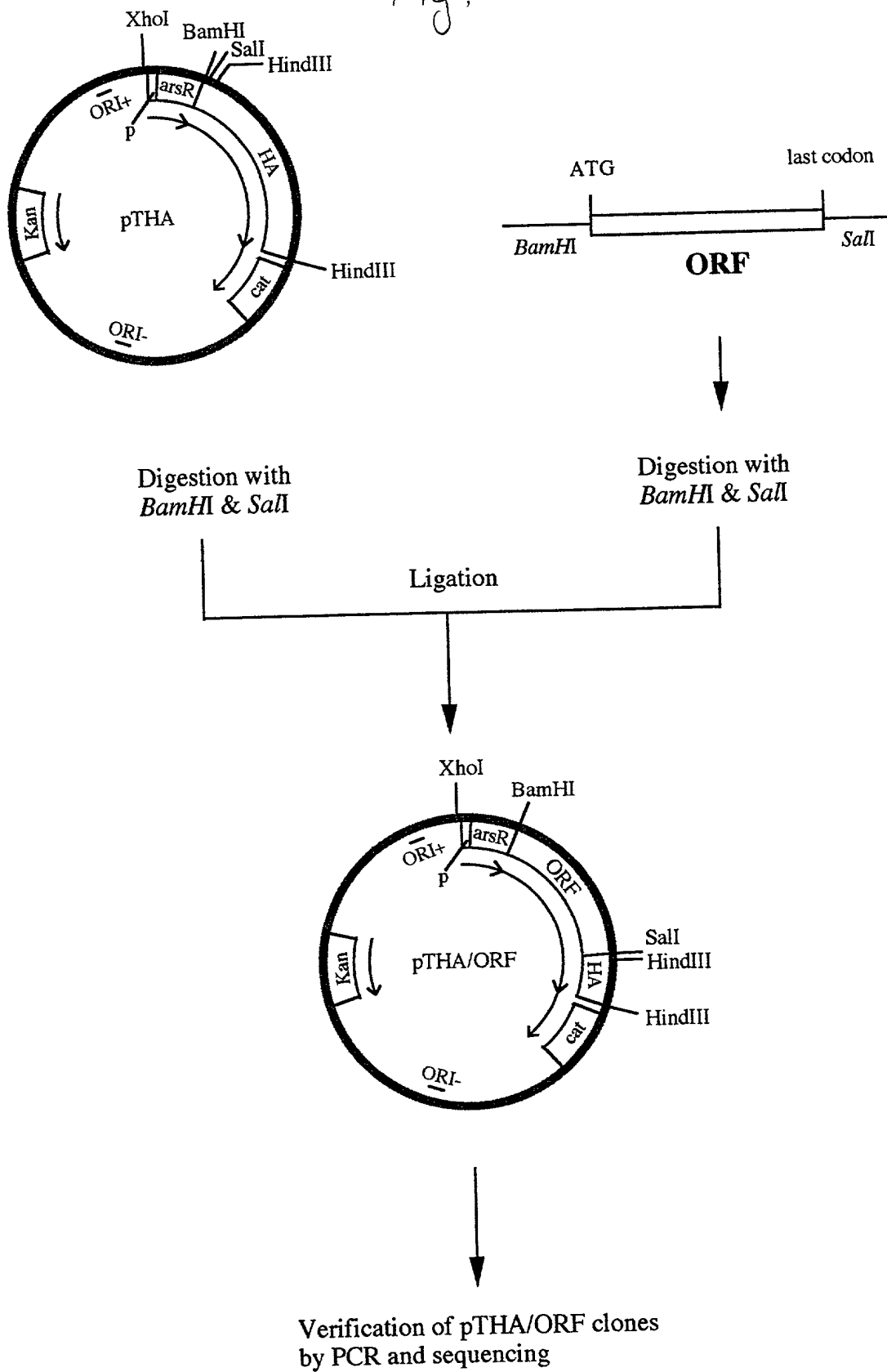
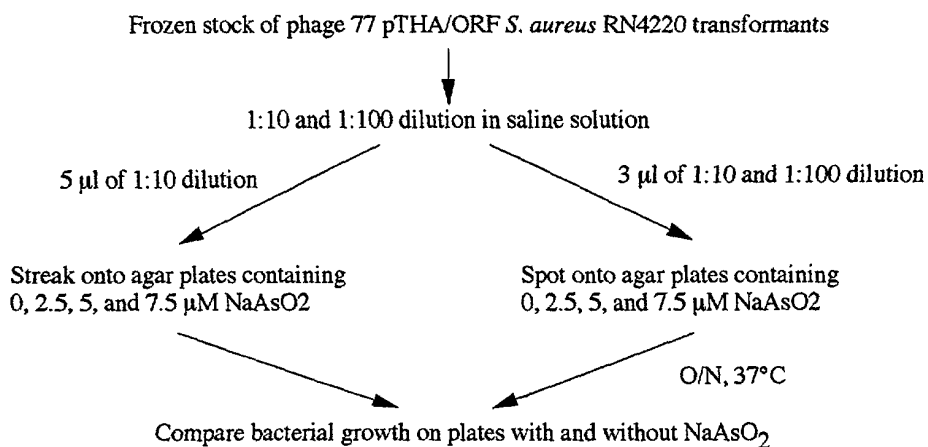


Fig. 3

A) Functional assay on semi-solid support media



B) Functional assay in liquid medium

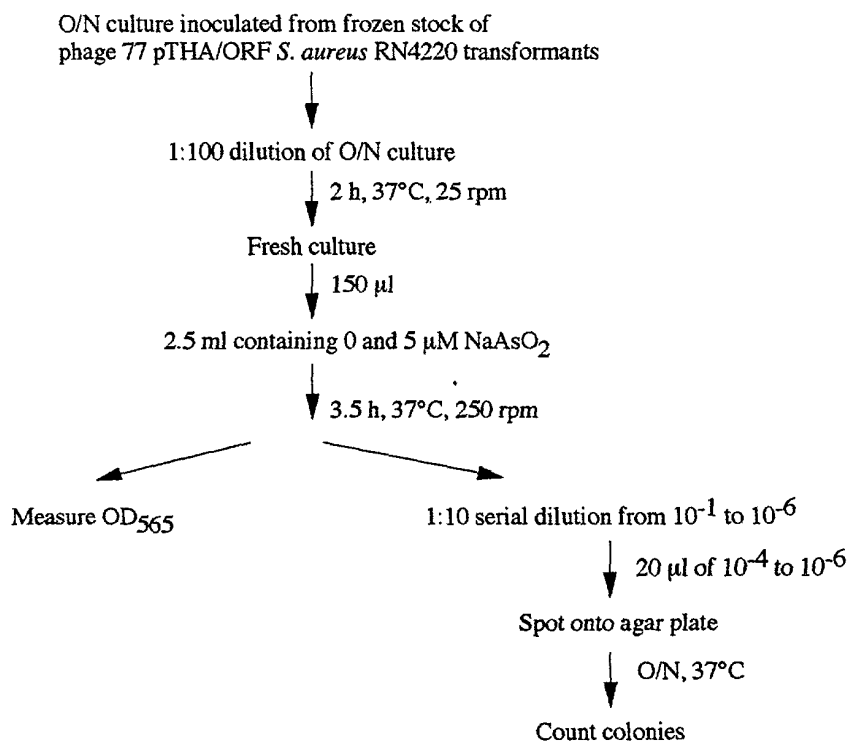
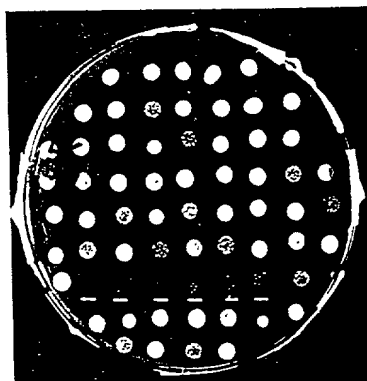
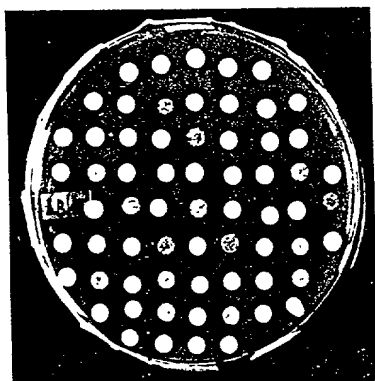
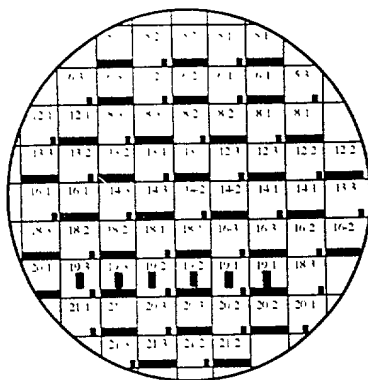


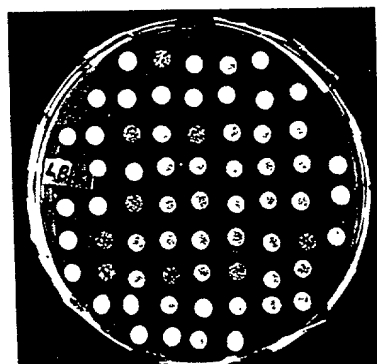
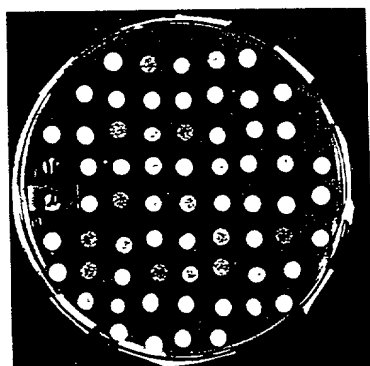
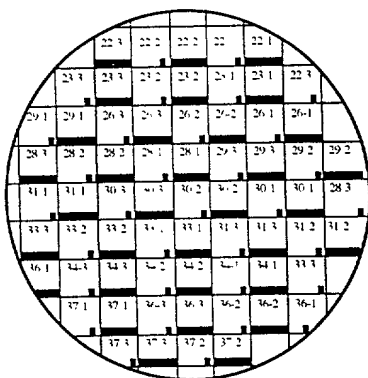
Fig. 4-1

A



5 μ M

B

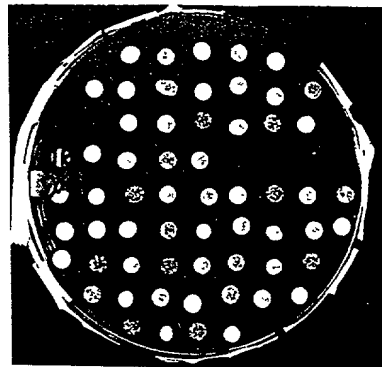
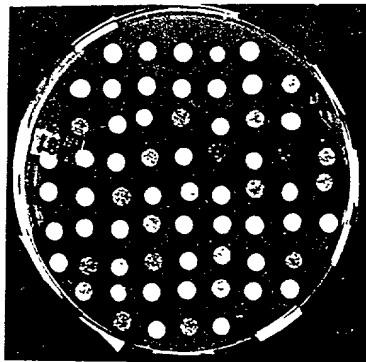
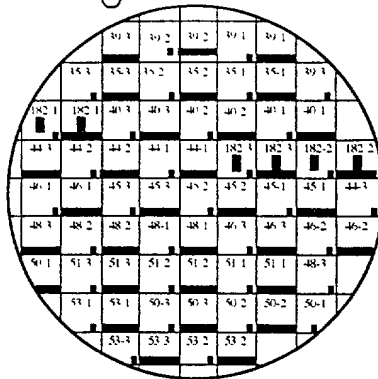


5 μ M

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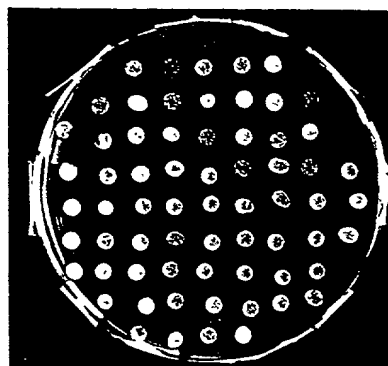
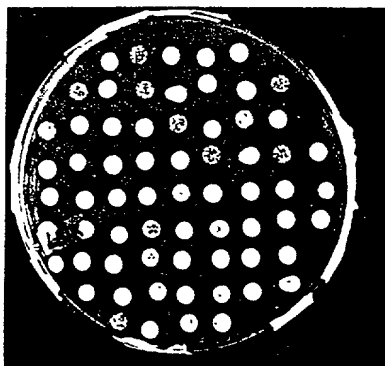
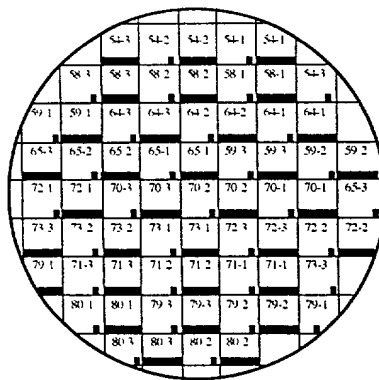
Fig. 4-2

C



5 μ M

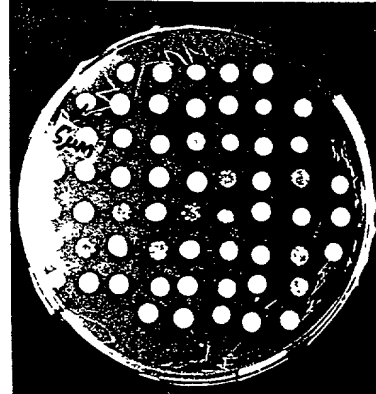
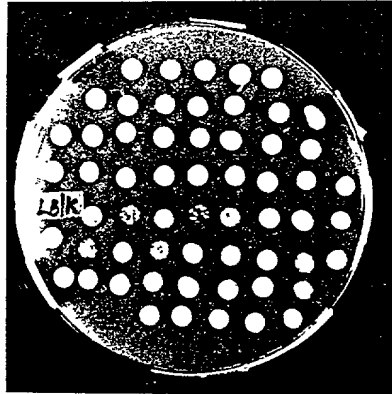
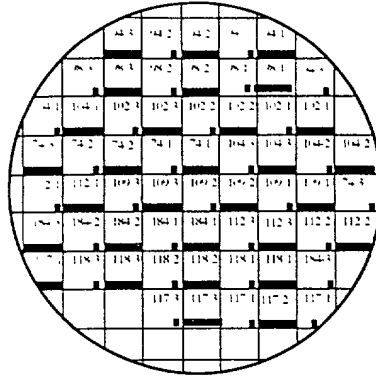
D



5 μ M

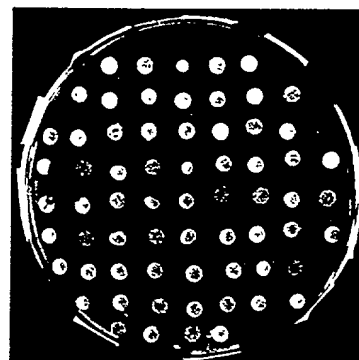
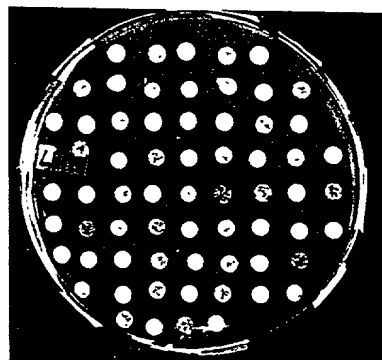
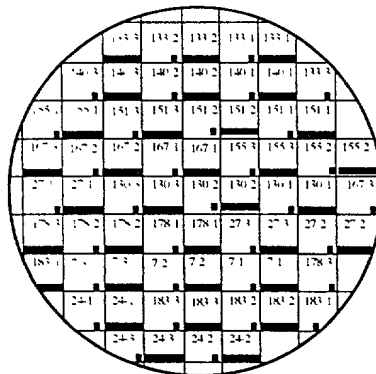
Fig. 4-3

E



5 μM

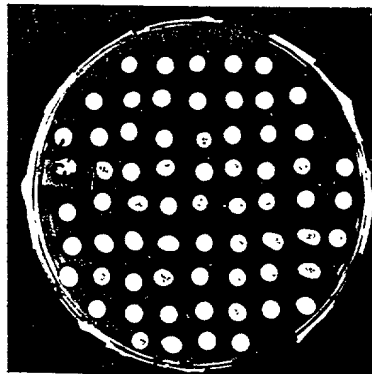
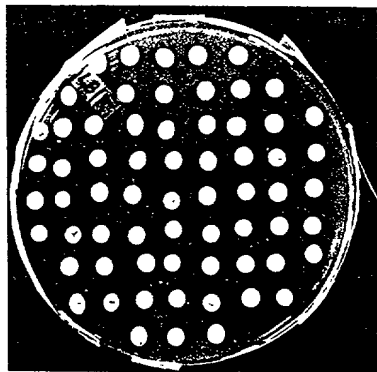
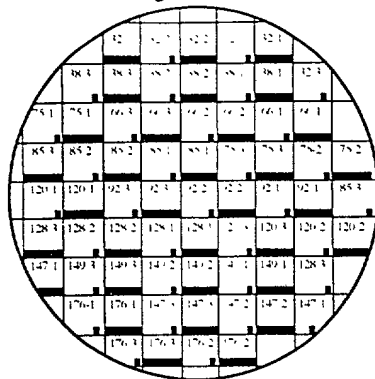
F



5 μM

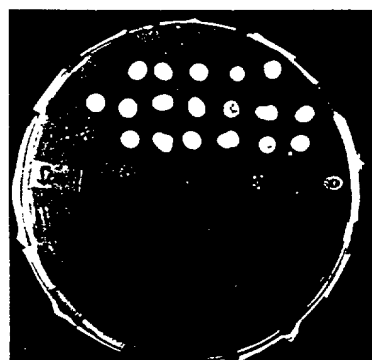
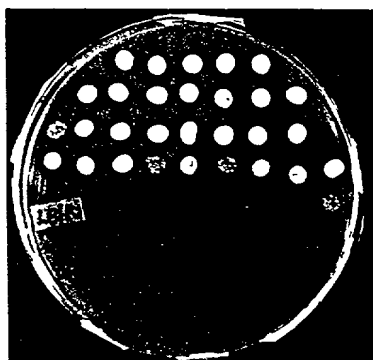
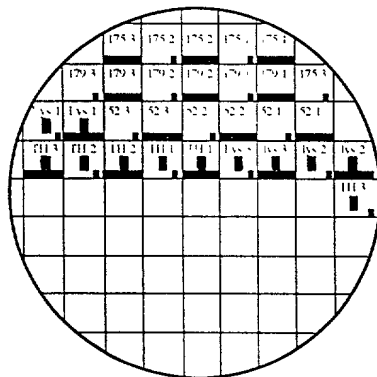
Fig. 4-4

G



5 μM

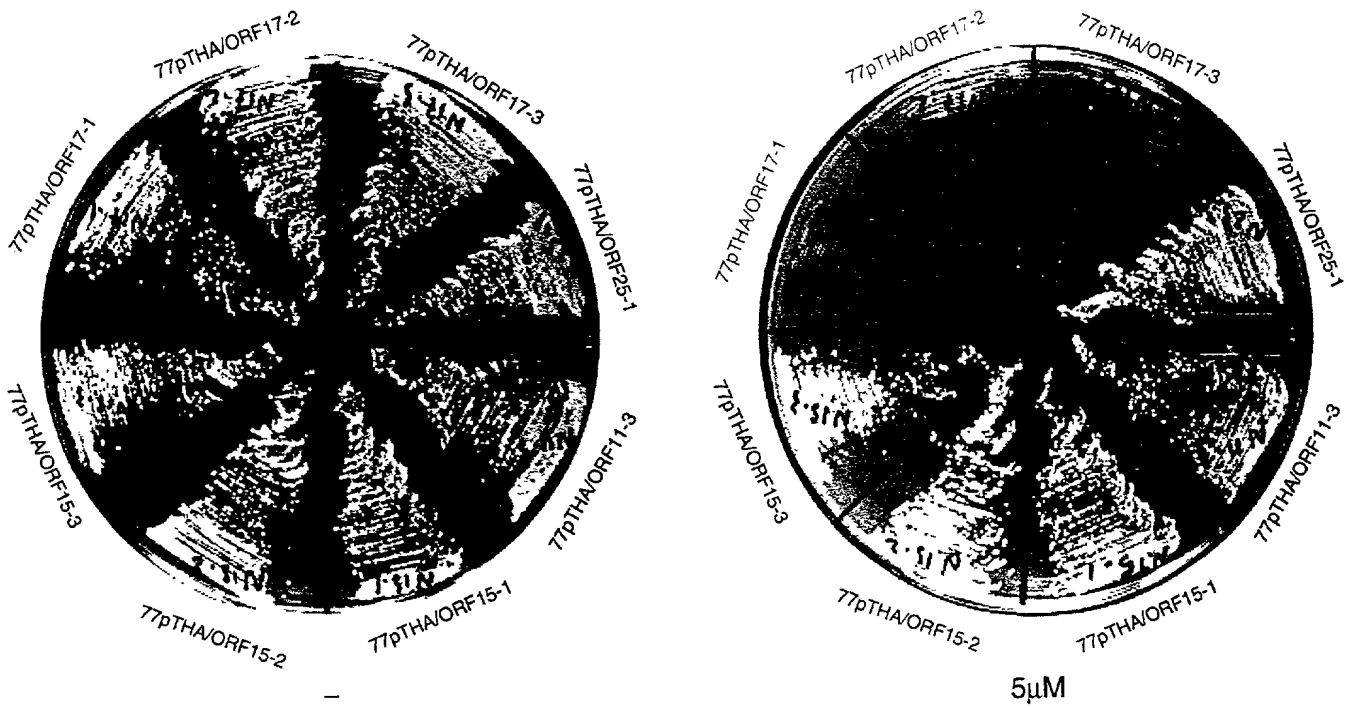
H



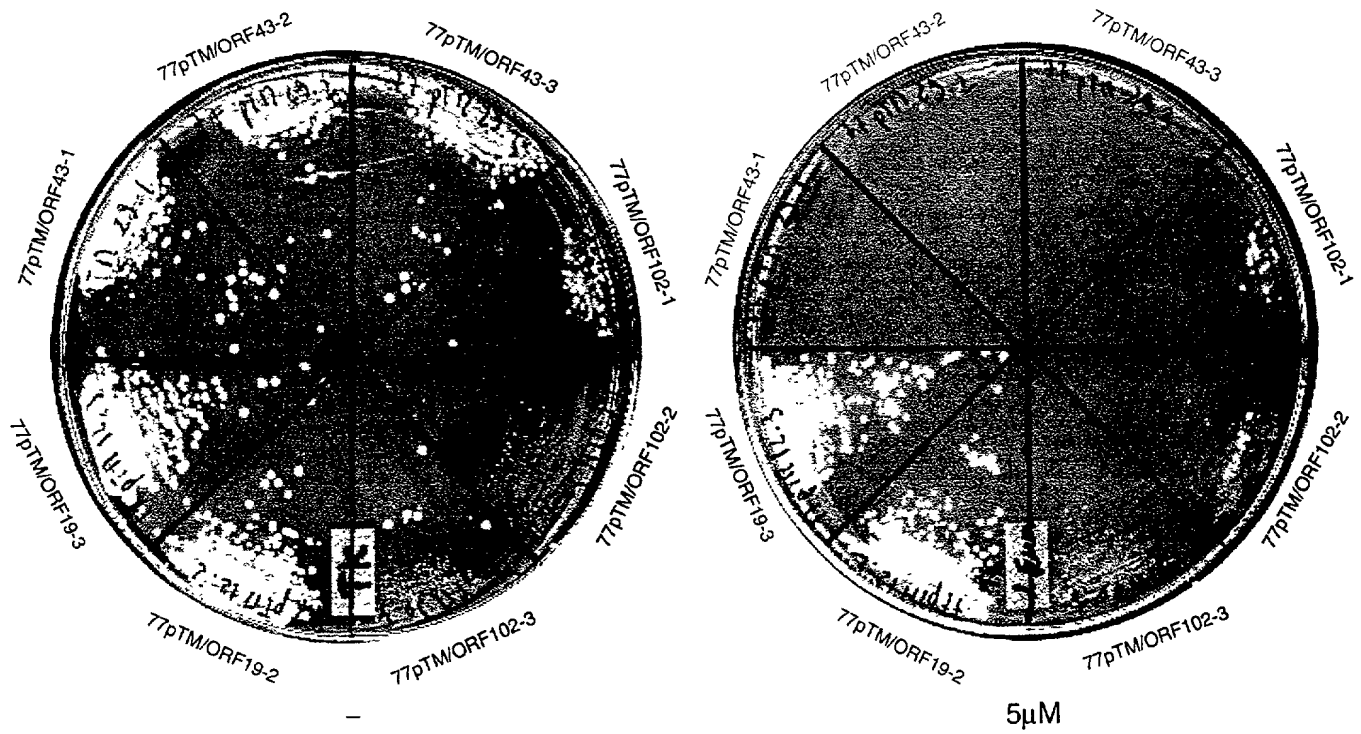
5 μM

Fig. 5-1

A



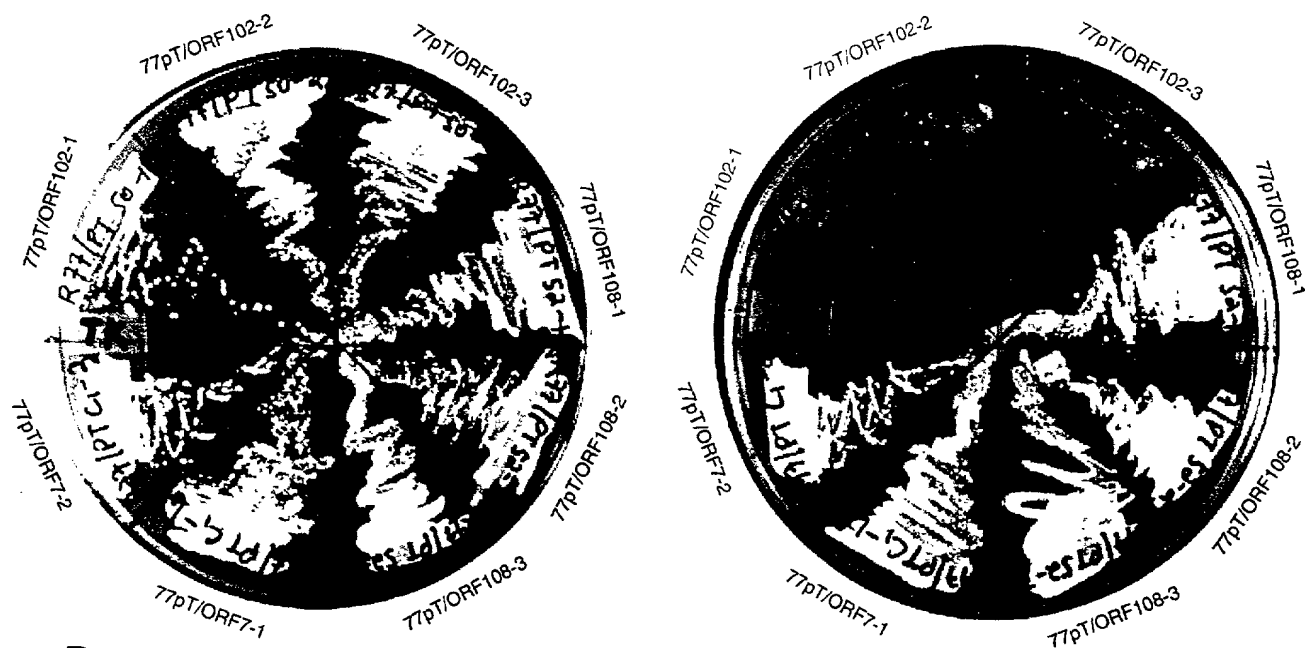
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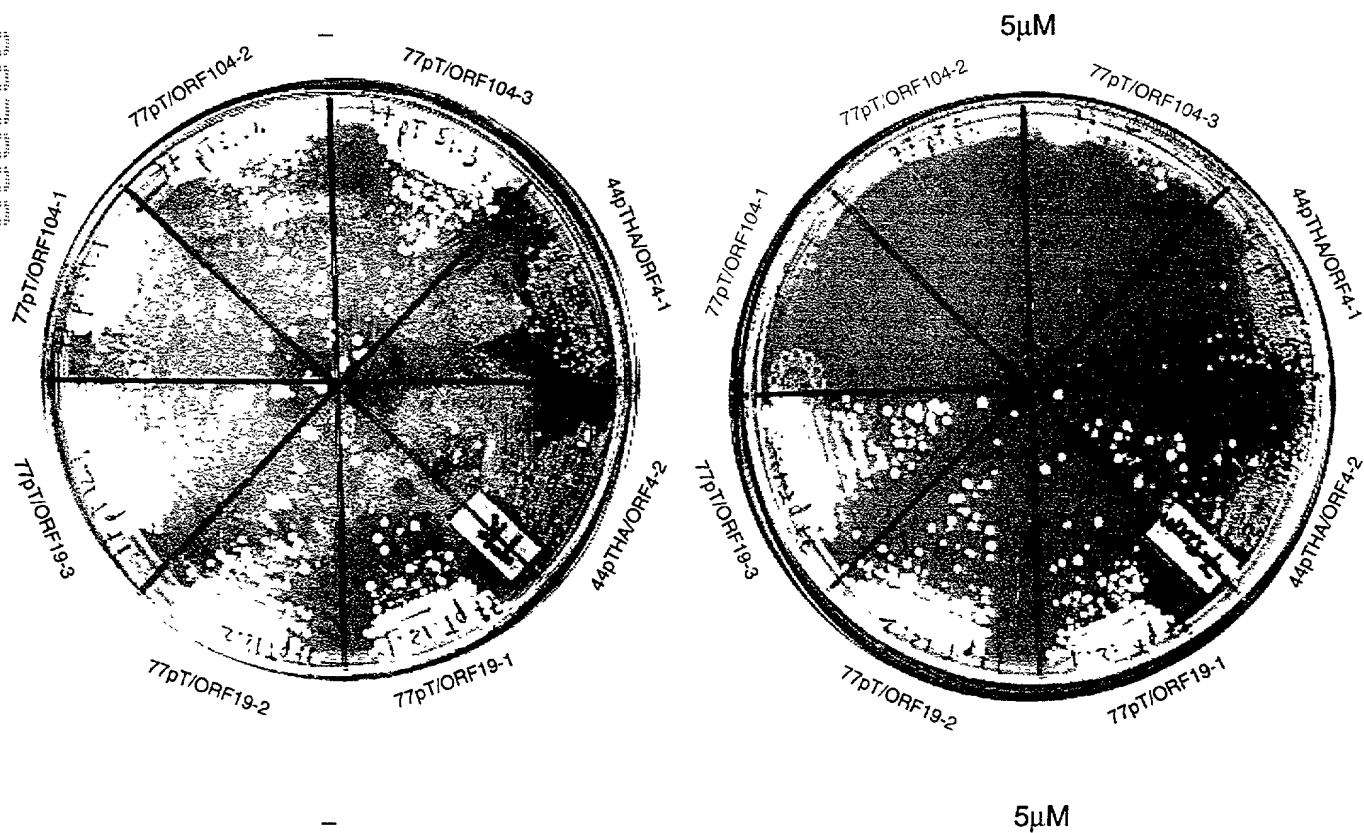
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Fig. 5-2

C

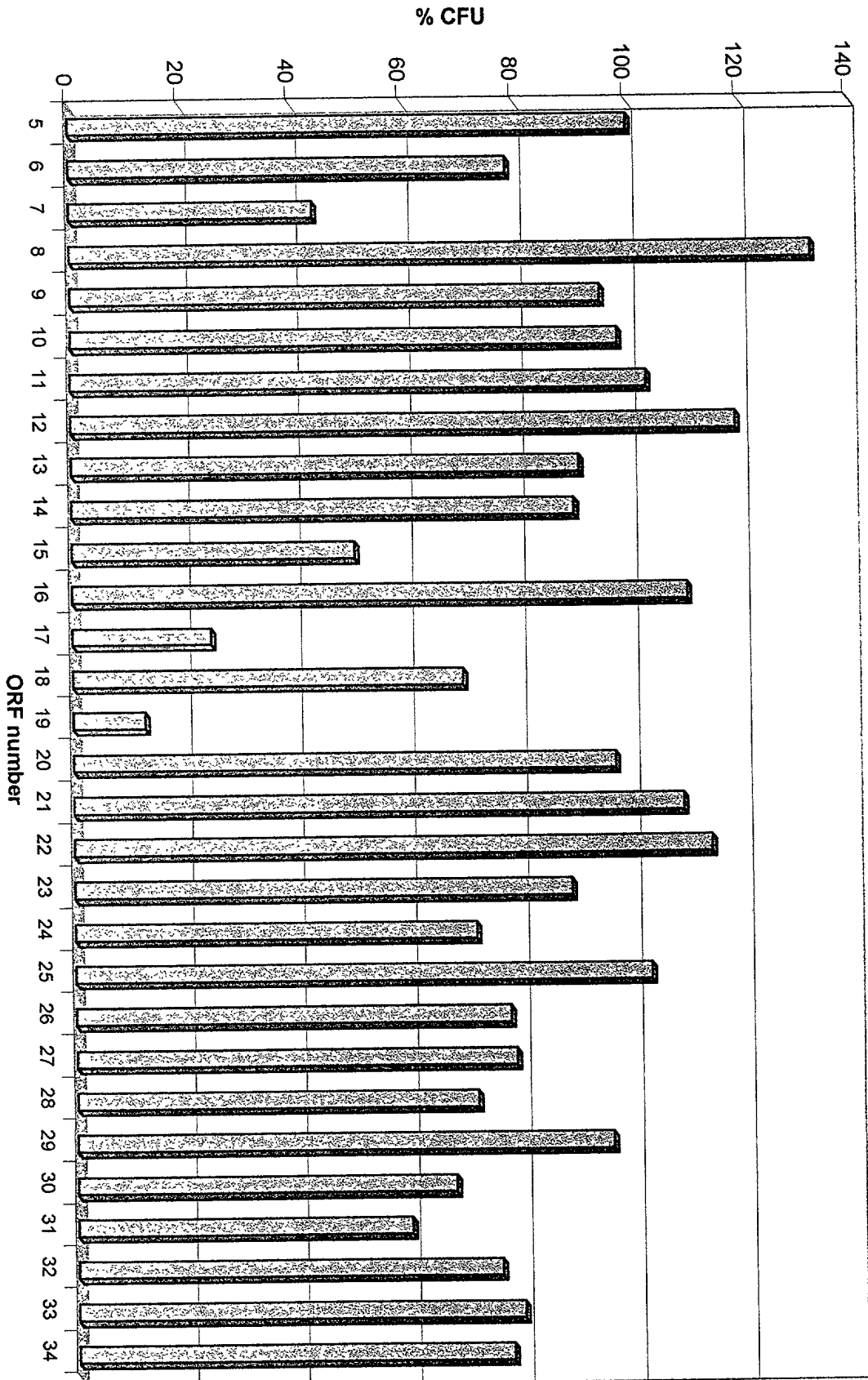


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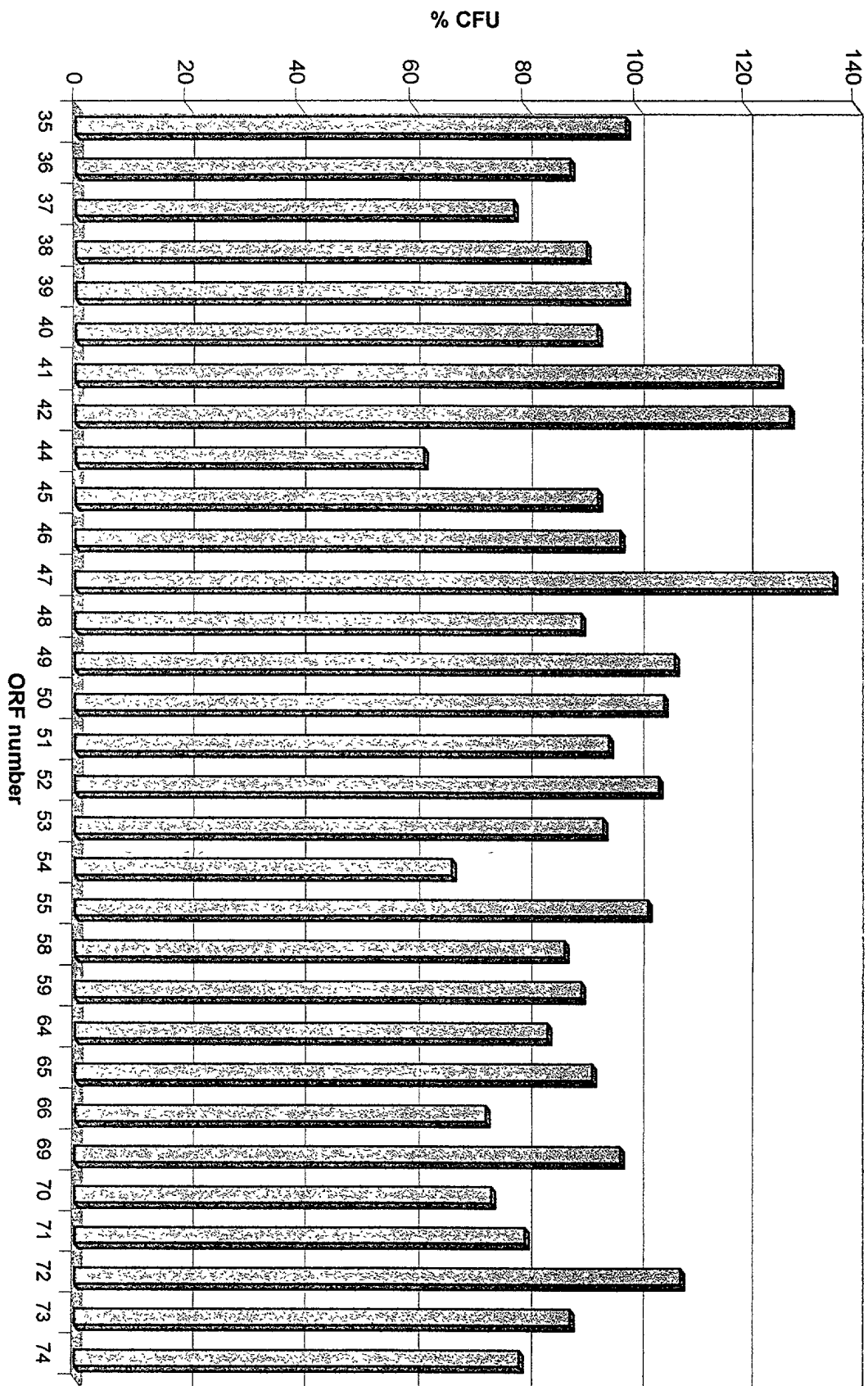
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Fig. 6-1



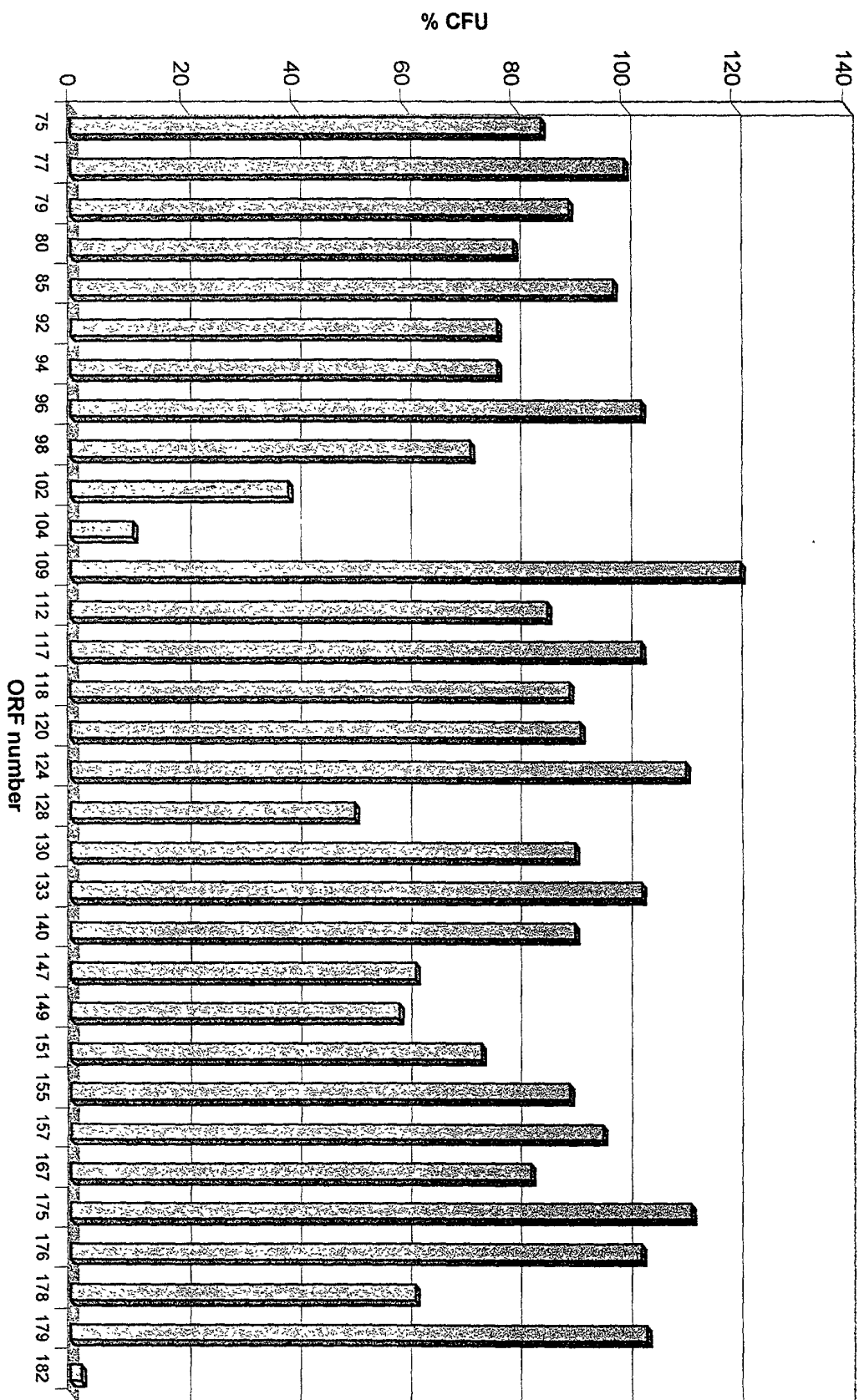
09407804, 097899

Fig. 6-2



09407304 092855

Fig. 6-3



09467804 092899

Table 1

PhageTech

Database

Genome Sequence

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30451	aacgctgaac	cttctaatac	gtttgaaaca	aagatttagac	attcaccttc	aataacaatt	aacaataa
30521	aatttgcaaa	tcctagcatt	acggacgtag	tagaagcaat	tagaaatgga	aactaaaaat	taattaaa

30591-35001 "46363"

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30591 gacggtat ttt aattatgaaa atcacaggac aagcgcaatt tactaaagaa acaaatcaag aaaagttt
30661 taacggctca gcagggtttc aagctggaga attcacagtg aaagttaaaa atattgaatt caatgata
30731 gaaaatagat atttcacaat cgtatttgaa aatgatgaag gcaaacaata taaacataat caatttgt
30801 cgccgtataa atatgatttc caagaaaaac aattgattga attagttact cgattaggta ttaagtta
30871 tcttcctagc ttagattttg ataccaatga tcttattggg aagttttgtc acttgggtatt gaaatgga
30941 ttcaatgaag atgaaggtaa gtatttttac gattttttcat ttattaaacc ttacaaaaag ggcgatga
31011 ttgttaacaa acctattccg aagacagata agcaaaaagc tgaagaaaat aacggggcac aacaacaa
31081 atcaatgtct caacaaagca atccatttga aagcagtggc caatttggtat atgacgacca agatttag
31151 ttttaagggtg tggtttaaat gcaatacatt acaagatacc agaaagataa cgacgggtact tattccgt
31221 ttgctactgg tgttgaactt gaacaaagtc acattgactt actagaaaac ggatatccac taaaagca
31291 agtagaggtt ccggacaata aaaaactatc tatagaacaa cgcaaaaaaa tattcgcaat gtgtagag
31361 atagaacttc actggggcga accagtagaa tcaactagaa aattattaca aacgaattg gaaattat
31431 aaggttatga agaaatcagt ctgcgcgact gttctatgaa agttgcaagg gagttaatag aactgatt
31501 agcgtttatg tttcatcatc aaatacctat gagtgtagaa acgagtaagt tgttaagcga agataaag
31571 ttattatatt gggctacaat caaccgcaac tgtgtaatat gcggaagcc tcacgcagac ctggcaca
31641 atgaagcagt cggcagaggc atgaacagaa acaaaatgaa ccactatgac aaacatgtat tagcgtta
31711 tcgcgaacat cacaacgagc aacatgcgat tggcgttaa tgcgttgatg ataaatacca cttgcatg
31781 tcgtggataa aagttgatga gaggtcfaat taactgctat cttggcggaa gagattagaa aaaggaatga atagacta
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31921 gtggagaaaa ttttaaaatc tccgttttag tgtctattac ccaggggctg taatgtaact ttaacttctc aatttcaa
31991 actaattgag ccttttttga tgtctattac ccaggggctg taatgtaact ttaacttctc aatttcaa
32061 ccagaaagtt tacttattgt ttctaggttg tgtcctgact ttaacattct ttaacaaaat tctaatac
32131 aaacaaatct ttgtttttct ataactttat taaagtatt taaaaactga ggagcataaa acttatta
32201 aattcctttt tttgttaagt aagacatgtc aaaagtttca tttaaaacc ctaaccttac taggttat
32271 attgaaattt cggttgattc tatatctaac ggagagtctt ttattaacgt gtccgatata ttcatacc
32341 cattctttgg gttaaaaacc gctctatatt taacggcagg atgtacttcg tgattcttta aatgtttt
32411 aagaatagca tcaattgggg ataattgttt aattatttca acaaatgaat tacttaaagt tttttacta atgtaaaa
32481 ctgtcatcca tagatgatgc tattagtttt gcgaacatat tctttaaagt tttttttag gtacagaa
32551 ttgaagcttc tagagcagga cctagaagag ctttgaattt ttcaaattct acttctctt gataaataac tttatcca
32621 tatttctttt ttaaattgtt ctttgaattt ttcaaattct acttctctt gataaataac tttatcca
32691 taaaggtgga atttcccaaa gacaagttcc caagttttag agaattgttc caccoccat ctaacgca
32761 cttcaataat tttatcaata cctttaccta aaataggatc cataattatt ctgaccaacc aagttactac tcaataat
32831 agcgataata aaattatacc agaaaggaga atcaacatga ctgacagcga aaagttaact tttgcagaaa taacatct
32901 cagcaaatgt cagatacgat aaccgactta ctgacagcga taatggttac tttgcaactt tatacaacgt tgtaaggg
32971 aagtaacaaa tacggatact gcacagcaag gaaccttacc aactttggtt atctaaaaat cgaaattatc aaagaagg
33041 actatatctc gtagaatttc gaaccttacc atgtacccct tgacgcaaat gtcaatacct attagcgcaa taattaata
33111 atgaagttaa aattctgtca ataccctat tagaatagat atattgtcgg gcaacccgac aatacagcta aaacaaaa
33181 ccctattgat acaatataaa tagaatagat atattgtcgg gcaacccgac aatacagcta aaacaaaa
33251 aagaatttat cgattactta acaaaaaaag cgggcaagca ttttaaacac aatacagcta aaacaaaa
33391 ttttattaaa gcaagatgga atcaagattt taggttgagg gatttttaaaa aggtgattga tatcaaaa
33461 gctgagtggc taaacacgga tagcgataaa taccttagac cagaaacact ttttggcagt aaatttga
33531 ggtacctcaa tcaaaaaata caaccaactg gcacggatca attggaacgc atggaagtag aagcgttgaa aaaatatc
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33671 cctactcatg tcgaaaaagg attgaatagt gagagatgtg ataaagacgg ttgcaaatgt gaaattatag aggaatat
33741 ctactaaaaa acacccgaat ggttacgagt taaacaacat attcaatcaa tcaaacgtta atcogtcttt aagagatg
33811 gcgaaacaag caacggaaga taaacaacat aaacaagtac acgctaaaca aacagcaata gagtacgt
33881 acagtcaaaa actacaagcc acaaaatgaa taatattgca aggttcatac ggaactggta aaagccac
33951 aaggcttctc tacaaaagaa cagtcaaagc taaagggcat acggttgctt ttatgcacat accaatgt
34021 agcatacgct atcgcaaaag atacaacaaa aatgcagtag agactacaga cgagctagtc agattgct
34091 atggatcgta tttacttgta cttagatgata tgggtgtaga caacactttt acaactaact ttagtgataa agaactaa
34161 gtgatattga tttacttgta cttagatgata tgggtgtaga caacactttt acaactaact ttagtgataa agaactaa
34231 cagcattggt gataacagag taggttaaaaa agaatgaaaa aaagagcaag ttaaaaaact aacttgagtg ttcagata
34301 caaaatatga actggcaacg tataaattcg gcatggtaac caaagaattt ttaaaaaact aacttgagtg ttcagata
34371 acgatttcag aactcataga tgaggcàcag ggcgatgaaa ataggttgta cgacctattt atccaaaa
34441 tacgctcaga aactcataga tgaggcàcag ggcgatgaaa ataggttgta cgacctattt atccaaaa
34511 ttgcagaacg tcatacacgc cccgctatcg tcgaatatta aggagtgtta aaaatgccga aagaaaaa
34581 ttacttatac cgagaagatg gcacagaaga tattaagggtc atcaagtata aagacaacgt aaatgagg
34651 tattcgctca caggagccca tttcagcgac gaaaagaaaa ttatgactga tagtgacctt aaacgatt
34721 aaggcgctca cgggcttcta tatgagcaag aattaggttt acaagcaacg atatttgata tttagagg
34791 gacgatgagt aaatacaacg aatgaatgtg aatggcacta attatgatca ttgatagcaa agtagagt
34861 gaatattacc aatattttag aagtaatatg gaaagattga attatgatca ttgatagcaa agtagagt
34931 tcgaattatt accaaaaacta gataaacaac gaaagattga atatattgca gacttcgctg tatatctc
35001 tggcaaacgt attgaagtta tcgacattaa aggtatgcc aaccgaagtag caaaaactta agctaaga

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35071   ttccagacata aatacagaaa cataaaactc aattggatat gtaaagcgcc taagtataca ggtaaaac
35141   ggattacgta cgaggaatta attaaagcaa gacgagaacg caaaagagaa atgaagtgat ctaattgca
35211   aacaagcata tataaatgca acgattgata taaggatacc tacagaagtt gaatatcagc attttgat
35281   tgtggataaa gaaaaagaag cgctggcaga ttacttatat aacaatcctg acgaaatact agagtatg
35351   aatttaaaaa ttagaaacgt aaatgtagag gtggaataaa tgggcagtggt tgtaatcatt aataataa
35421   catataaatt taacaatttt gaaaaaagaa ataatggcaa agcgtgggat aaatgctgga attgtttc
35491   aacgtgttag aggttgttgg gagttttcag aagctttaga cgcgccttat ggcatgcacc taaaagaa
35561   tagagaaatg aaacaaatgg aaaagattaa acaagcgaga ctggaacgtg aattggaaag agagcgaa
35631   aaagaggctg agctacgtaa gaagaagcca catttgttta atgtacctca aaacattca cgtgatcc
35701   actggttcga tgtcacttat aaccaaatgt tcaagaaatg gagtgaagca taatgagcat aatcagta
35771   agaaaagtag atatgaacaa aacgcaagac aacgttaagc aacctgcgca ttacacatac ggcgacat
35841   aaattataga ttttattgaa caagttacgg cacagtaccc accacaatta gcattcgcaa taggtaat
35911   aattaaatac ttgtctagag caccgttaaa gaatggctcat gaggatttag caaaggcgaa gttttacg
35981   gatagagtat ttgacttgtg ggagtgatga ccatgacaga tagcggacgt aaagaatact taaaacat
36051   tttcggctct aagagatatc tgtatcagga taacgaacga gtggcacata tccatgtagt aaatggca
36121   tattactttc acggtcatat cgtgccaggt tggcaagggtg tgaaaaagac atttgataca gcggaaga
36191   ttgaaacata tataaagcaa agtgatttgg aatgatgaga acagaagcaa ctaactttat tttaaaag
36261   cggaacaatg gaaaatcaaa attgaaaaag aaatgaattt acctgaactt atccaatggg cttgggat
36331   ccccaagtta tcaggtaata agtttcaatg tatgtatcaa ttaacgataa atttactggt caagagga
36401   gttgatagca tcttatgtaa tgtgacttga aatgagatta gatgaattaa tttaatgggc gcgagaaa
36471   tataacaatg aaaatcaaag ttaaaaaaga aatgagatta gatgaattaa tttaatgggc gcgagaaa
36541   ccggtcttat cacaaggaaa aatatTTTTT tcaacaggat ttagtgatgg attcgttcgt ttcatcc
36611   atacaaataa gtgttcgacg tcaagtttta ttccaattga tatcccttc atagttgata ttgaaaaa
36681   agtaacggaa gagactaagg ttgatagggt gattgaatta ttcgagattc aagaaggaga ctataact
36751   acactatatg agaacactag tataaaagaa tgtttatatg gcagatgtgt gctaccaaaa gcattcta
36821   tcttaaagca tgacctaatc atgacgttaa tctggaaaga tggggagttg ctagtatgat gttgaaat
36891   aaagcttggg ataaagataa aaaagttatg agtattattg acgaaatcga ttttaatatg gggtagat
36961   tgaattcaac aggttataaa agtttcaatg aagtaaaaat attacaatac acaggattta aagatgtg
37031   cggtgtggag atttatgaag gggatattgt tcaagattgt tattcgagag aagtaagttt tatcgagt
37101   aaagaaggag ctttttatat aacttttagc aatgtaactg aattactaag tgaaaatgac gatattat
37171   aaattgttgg aatatTTTTT gaaaatgaga tgctattgga gggtatgaga tgacgttcac cttatcag
37241   gaacaatata aaaatctttg tactaactct aacaagttat tagataaact tcacaaagca ttaaaaga
37311   gtgaagagta caagaagcaa cgagatgagc ttattgggga tatagcgaag ttacgagatt gtaacaaa
37381   tctagagaag aaagcaagcg catgggatag gtattgcaag agcgttgaaa aagatttaat aaacgaat
37451   ggtaacgatg atgaaagagt taaattcggg atggaattaa acaataaaaat ttttatggag gatgacac
37521   atgaataatc cgaaaaaaat cgcagagtcg gacgtgtata agaaaagcgca ttagtattgt agatataaaa
37591   gggtgtctaaa agagattgag gacgtgtata agaaaagcgca ttagtattgt agatataaaa
37661   aaatgctatt caacattcag ttaaaagaag tattgaactt gatgaagcag acattacaag taactattt
37731   gttgtctata aatatgagga ggaataggaa aatgactaac acattacaag taactattt
37801   gctagaatgc ccgaacgaaa tcataagacg gatgcaggtt atgacatatt ctcagctgaa actgtcgt
37871   tcgaaccaca agaaaaagca gtgatcaaaa cagatgtagc tgtgagtata ccagagggct atgtcggg
37941   attaactagt cgtagtgggt taagtagtaa aacgtattta gtgattgaaa caggcaagat agacgcgg
38011   tatcatggca atttagggat taatatcaag aatgatgaag aacgtgatgg aatacccttt ttatatga
38081   atatagacgc tgaattagaa accaaatcaa caaagcgtt tttcagaacg ttttgaggaa ggttaactatg
38151   aagaggcata agaagagttt accaaatcaa caaagcgtt tttcagaacg ttttgaggaa ggttaactatg
38221   tggacaccgg aactaaagca agtgaggaa ttcgaaaagt tttcagaacg ttttgaggaa ggttaactatg
38291   gtacgggagt gtaaagacat cttagatcga gacgaccaca tgaacatatt actgtggcta gagataatca
38361   aacattcaaa gattcaacag agaagaagcg aaagagaagt acgaggcaca agttaaaga gatgcagt
38431   gttattgagg cagagagtaa agaagaagcg aaagagaagt acgaggcaca agttaaaga gatgcagt
38501   ttaaagtggg tcagttgtat gaaaaatataa gggagtgtgg gaaatgacgg atgttaaaat taaaacta
38571   tcaggtggag tttattttgt aaaaacagct gaaccttttg aaaaatatgt tgaaagaatg acgagttt
38641   atgggtatat ttacgcaagt actataatca agaaaccaac gtatatataa acagatacga ttgaatca
38711   cacacttatt gaggagcatg gaaaatgaat cagctgagaa ttttattaca tgacggtagt agtttgat
38781   tacatgaaga tgaattattt aacgaaatag tatttgtttt ggacaatttt agaaatgatg atgactat
38851   aacgatagaa aaagattatg gcagagaact tgtattgaac aaagggtata tagttgggat caatgttg
38921   gaggcagatg atgattaaca tacctaaaat gaaattcccg aaaaagtaca ctgaaataat caaaaaat
38991   aaaaataaag cacctgaaga aaaggctaag attgaagatg attttattaa agaaattaaa gataaaga
39061   gtgaatttta cagtccctac atggctaata tgaatgaata tgaatgaata gctatgttaa gaatgatg
39131   tagtttaatt gatactggag atgacaatga ttttcggtat attcgcattg ctacttgtaa tcacattgcc tatctata
39201   tattgttggg atactgtcat ttttcggtat caaggaacta ttacagataa atataacaag agacaaga
39271   gtggctagtt accaacacaa agaattacat acaaaacaag cattgaaaat tccgacttat tattcaaa
39341   aagaagacaa gttctatatt gtattagaca gttaaaagta ggcgataagg tagaagttaa aacaatcg
39411   gaaatttgat agcgcagata tacaagctag gttaaaagta ggcgataagg tagaagttaa aacaatcg
39481   tatagaatac actttttaaa tttatatccg gtcttatacg aagtaaaaga ggtagataaa caatgatt

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39551	acaaatacta	agactattat	tcttactagc	aatgtatgag	ttaggtaagt	atgtaactga	gcaagtgt
39621	attatgatga	cggctaata	tgatgtagag	gcgcgcgagt	attacgtctt	tcgagcggag	gtgagtga
39691	aatgagaata	tttatttatg	atttgatcgt	tttgctgttt	gctttcttaa	tatccatata	tattattg
39761	gatggagtga	taataaatgc	attaggaatt	tttggtatgt	ataaaattat	agattccctt	tcagaaaa
39831	ttataaagag	gtagataaaa	atgaacgagc	aaataatagg	aagcatatat	acttttagcag	gaggtggt
39901	gctttattca	gttaaagaga	tttttaggta	ttttacagat	tctaacttac	aacgtaaaaa	aatcaatt
39971	gaacaaatat	atccgatata	tttagattgt	tttaaaaagg	ctaaaaagat	gattggagct	tatattat
40041	caacagaaca	gcatgaattt	ttagattttt	ttgatattga	agtctttaat	aatttagata	agcaaagt
40111	aaaagcgtat	gaaaatgtta	ttggatttag	acaaatgatt	aatttatcaa	atagagttaa	ggcaatgg
40181	gatttttaaga	tgagttttcaa	caatgaattt	agtacaaatc	agattttttt	taatccttct	tttgttat
40251	aaacaattgc	tattataaat	gaatatcaaa	aagatatatc	ttatttaaaa	aatataatta	ataaaaatg
40321	tgaaaataga	gcttataatc	atattgatag	ttttatcact	tcagagtacc	gacgaaaaat	aaacgatt
40391	aatctttatc	ttgataaatt	tgaagaacag	tttagtcaaa	agtttaaaat	aaacagaact	tcgataaa
40461	aaagaattat	tattaattta	aacaagagga	gatttaaatg	atgtggatta	ctatgactat	tgtatttg
40531	atattgctat	tagtttgtat	cagtattaat	agtgatcgtg	caagagagat	acaagcactt	agatatat
40601	atgattatct	acttgatgaa	gtagttaaaa	ctaaagggtg	caacgggtta	gaagaataca	ggattgaa
40671	gaagcgaatg	aataacgata	ttaaaaagta	atztatatta	tcggagggtat	tgcatggaat	gataaaga
40741	gagaaacacg	atatcaaaaa	gcttgaagaa	tacattcagc	acatcgataa	ctatcgaa	gagttgaa
40811	tgcgagaata	tgaattactt	gaaagtcag	aaccagataa	tgccggagct	ggcaaaagta	atgtgccg
40881	taaccgcgatt	gaacgatgtg	caataaagaa	gttttagtat	aacaggtaca	atacatgaag	aaatatag
40951	aacgggtgtag	atagattgat	aggtgaaagt	gatgaggata	cgcttgagtt	attaagggtt	agattattg
41021	attgtcctat	tggttggtat	gaatgggaag	atatagcaca	ttacttttgt	acaagtaaga	caagtata
41091	acgtagaagg	aatgcactga	tcgataagtt	agcaaagtat	attggttatg	tgtagcggac	ttttaccc
41161	tgtaagtccg	cattaaaaca	gtttattatg	ttagtatcag	attaatat	aaagttatta	aatgctaa
41231	cgacgcgatga	acaagaggcg	catcactatg	tgatgtgtct	ttttatttat	gaggtatgaa	catgttca
41301	ctaattgtaa	atacattact	acacatcaag	tatagatgag	tcttgatact	acttaagtta	tataagggt
41371	aacattatga	tgactaaaga	cgaacgtata	cgattctata	agtctaaaga	atggcaaata	acaagaaa
41441	gagtgcctaga	aagagataat	tatgaatgtc	aaacaatgtaa	gagagacggc	aagttaacga	catatgac
41511	aagcgacgct	aagtcgtttg	atgtagatca	tatatattcg	ctagaacatc	atccggagtt	tgctcatg
41581	ttaaacaatt	tagaaacact	gtgtattaaa	tgtcacaa	aaaaagaaaa	gagatttata	aaaaaaga
41651	ataaatggaa	agacgaaaaa	tggtaaatac	ccccgggtca	aaaaaatcaa	aagcgatc	

Table 2

1st position (5' end) ↓	2nd position				3rd position (3' end) ↓
U	U	C	A	G	
U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G
C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G
A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G
G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G

Figure 3-16 The genetic code. Sets of three nucleotides (*codons*) in an mRNA molecule are translated into amino acids in the course of protein synthesis according to the rules shown. The codons GUG and GAG, for example, are translated into valine and glutamic acid, respectively. Note that those codons with U or C as the second nucleotide tend to specify the more hydrophobic amino acids

Table 3

77ORF017 sequence

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23982 atgacgcataatatagaaaaacgcattaataaattaaaaacttct
1   M T H N I E K R I N K L K T S
23937 ggaaatccaaaattttaaaaagtttagattcagatattcactattta
16  G N P K F K K L D S D I H Y L
23892 ctcaagagatttgaagggtgaaaaaaaccataaagggtttttatcca
31  L K R F E G E K N H K G F Y P
23847 aagttttaacaaggagaaatagttttttagatttcggtataaac
46  K F K Q G E I V F V D F G I N
23802 gttaataaagaatttttctaattcacactttgcaatagtgatgaat
61  V N K E F S N S H F A I V M N
23757 aaaaatgattctaatacggaggatatagtaaatgttattccctta
76  K N D S N T E D I V N V I P L
23712 tcctctaagaaaaacaaaaagtattttaaagatgaattttgatttg
91  S S K E N K K Y L K M N F D L
23667 aaatgggagattatttttaagattgtttttaaatattaagcgcg
106 K W E Y Y L R L F L N L I S A
23622 caaaataattcagctatattaaaagaagttttcgataaaaaaatac
121 Q N N S A I L K E V F D K K Y
23577 caaaaaaacacacagaattcatcactaaagattattttattgaa
136 Q K N N T E F I T K D Y F I E
23532 tttatatctgatagttttagaaattgaaaataaattaaataaaaatt
151 F I S D S L E I E N K L N K I
23487 gacagaaacattaataacatagtatcagcaattgataaggtaaaa
166 D R N I N N I V S A I D K V K
23442 aaattaaaaggtaatatgttacgcttgataaattctttccagccg
181 K L K G N S Y A C I N S F Q P
23397 attagtaagtttcgcataagaaaagttttaccccaaaaaattaaa
196 I S K F R I R K V L P Q K I K
23352 aatccagtaatatagattcttcggatattatgttactgataaataga
211 N P V I D S S D I M L L I N R
23307 attaataataatatattgcagatccctgatataagatga 23269
226 I N N N I L Q I P D I R *

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662267092040

Physico-chemical parameters of ORF 77ORF017

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1      MTHNIEKRIN KLKTSGNPKF KKLDSDIHYL LKRFEGEKNH KGFYPKFKQG EIVFVDFGIN
61     VNKEFSNSHF AIVMNKNSDN TEDIVNVIPL SSKENKKYLK MNFDLKWEYY LRLFLNLISA
121    QNNSAILKEV FDKKYQKNNT EFITKDYFIE FIDSLEIEN KLNKIDRNIN NIVSAIDKVK
181    KLKGSYACI NSFQISKFR IRKVLPQKIK NPVIDSSDIM LLINRINNNI LQIPDIR
  
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Number of amino acids: 237
 Average molecular weight (Daltons): 27887.38
 Mean amino acid weight (Daltons): 117.67
 Monoisotopic molecular weight (Daltons): 27869.83
 Mean amino acid monoisotopic weight (Daltons): 117.59

Amino acid composition

Acid	Symbol	Number	%	Average % in Swissprot	Acid	Symbol	Number	%	Average % in Swissprot
Ala	A	5	2.11%	7.58%	Cys	C	1	0.42%	1.66%
Asp	D	14	5.91%	5.28%	Glu	E	13	5.49%	6.37%
Phe	F	16	6.75%	4.09%	Gly	G	6	2.53%	6.84%
His	H	4	1.69%	2.24%	Ile	I	29	12.24%	5.81%
Lys	K	33	13.92%	5.95%	Leu	L	19	8.02%	9.42%
Met	M	4	1.69%	2.37%	Asn	N	30	12.66%	4.45%
Pro	P	7	2.95%	4.9%	Gln	Q	6	2.53%	3.97%
Arg	R	8	3.38%	5.16%	Ser	S	17	7.17%	7.12%
Thr	T	5	2.11%	5.67%	Val	V	11	4.64%	6.58%
Trp	W	1	0.42%	1.23%	Tyr	Y	8	3.38%	3.18%

Number of acidic (negative) amino acids (ED): 27 11.39%
 Number of basic (positive) amino acids (KR): 41 17.30%
 Total charge (KRED): 68 28.69%
 Net charge (KR - ED): 14 5.91%
 Theoretical pI: 10.01
 Total linear charge density: 0.30
 Average hydrophobicity: -5.37
 Ratio of hydrophilicity to hydrophobicity: 1.41
 Percentage of hydrophilic amino acid: 57.81%
 Percentage of hydrophobic amino acid: 42.19%
 Ratio of %hydrophilic to %hydrophobic: 1.37

77ORF019 sequence

39851 atgaacgagcaaataaataggaagcatatatacttttagcaggaggt
1 M N E Q I I G S I Y T L A G G
39896 gttgtgctttatttcagttaaagagatttttaggtattttacagat
16 V V L Y S V K E I F R Y F T D
39941 tctaacttacaacgtaaaaaaatcaatttagaacaatatatccg
31 S N L Q R K K I N L E Q I Y P
39986 atatatttagattgttttaaaaaaggctaaaaagatgattggagct
46 I Y L D C F K K A K K M I G A
40031 tatattattccaacagaaacagcatgaatttttagattttttgat
61 Y I I P T E Q H E F L D F F D
40076 attgaagtctttaataatttagataagcaaagtaaaaagcgtat
76 I E V F N N L D K Q S K K A Y
40121 gaaaatgttattggatttagacaaatgattaatttatcaaataga
91 E N V I G F R Q M I N L S N R
40166 gttaaggcaatggaagattttaagatgagtttcaacaatgaattt
106 V K A M E D F K M S F N N E F
40211 agtacaaatcagattttttttaatccttcttttggtatggaaaca
121 S T N Q I F F N P S F V M E T
40256 attgctattataaatgaatatcaaaaagatatatcttattttaaaa
136 I A I I N E Y Q K D I S Y L K
40301 aatataattaataaaaatgaatgaaaatagagcttataatcatatt
151 N I I N K M N E N R A Y N H I
40346 gatagttttatcacttcagagtaccgacgaaaaataaacgattat
166 D S F I T S E Y R R K I N D Y
40391 aatctttatcttgataaatttgaagaacagtttagtcaaaagttt
181 N L Y L D K F E E Q F S Q K F
40436 aaaataaacagaacttcgataaaaagaaagaattattattaattta
196 K I N R T S I K E R I I I N L
40481 aacaagaggagattttaaatga 40501
211 N K R R F K *

66226-77ORF019

Physico-chemical parameters of ORF 77ORF019

1 MNEQIIGSIY TLAGGVVLYS VKEIFRYFTD SNLQRKKINL EQIYPIYLDK FKKAKKMIGA
61 YIIPTEQHEF LDFFDIEVFN NLDKQSKKAY ENVIGFRQMI NLSNRVKAME DFKMSFNNEF
121 STNQIFFNPS FVMETIAIIN EYQKDISYLK NIINKMNENR AYNHIDSFIT SEYRRKINDY
181 NLYLDKFEEQ FSQKFkinRT SIKERIIINL NKRRFK

Number of amino acids: 216
Average molecular weight (Daltons): 26026.06
Mean amino acid weight (Daltons): 120.49
Monoisotopic molecular weight (Daltons): 26009.34
Mean amino acid monoisotopic weight (Daltons): 120.41

Amino acid composition

Acid	Symbol	Number	%	Average % in Swissprot	Acid	Symbol	Number	%	Average % in Swissprot
Ala	A	7	3.24%	7.58%	Cys	C	1	0.46%	1.66%
Asp	D	10	4.63%	5.28%	Glu	E	16	7.41%	6.37%
Phe	F	19	8.80%	4.09%	Gly	G	5	2.31%	6.84%
His	H	2	0.93%	2.24%	Ile	I	28	12.96%	5.81%
Lys	K	22	10.19%	5.95%	Leu	L	12	5.56%	9.42%
Met	M	7	3.24%	2.37%	Asn	N	23	10.65%	4.45%
Pro	P	3	1.39%	4.9%	Gln	Q	10	4.63%	3.97%
Arg	R	11	5.09%	5.16%	Ser	S	13	6.02%	7.12%
Thr	T	7	3.24%	5.67%	Val	V	7	3.24%	6.58%
Trp	W	0	0.00%	1.23%	Tyr	Y	13	6.02%	3.18%

Number of acidic (negative) amino acids (ED): 26 12.04%
Number of basic (positive) amino acids (KR): 33 15.28%
Total charge (KRED): 59 27.31%
Net charge (KR - ED): 7 3.24%
Theoretical pI: 9.52
Total linear charge density: 0.28
Average hydrophobicity: -4.84
Ratio of hydrophilicity to hydrophobicity: 1.37
Percentage of hydrophilic amino acid: 54.17%
Percentage of hydrophobic amino acid: 45.83%
Ratio of %hydrophilic to %hydrophobic: 1.18

77ORF043 sequence

```
29304 atgtattacgaaataggcgaaatcatacgcaaaaatattcatgtt
1   M Y Y E I G E I I R K N I H V
29349 aacggattcgattttaagctattcatttttaaaaggcatatgggc
16  N G F D F K L F I L K G H M G
29394 atatcaatacaagtttaaagatatgaacaacgtaccaattaaacat
31  I S I Q V K D M N N V P I K H
29439 gcttatgtcgtagatgagaatgacttagatatggcatcagactta
46  A Y V V D E N D L D M A S D L
29484 tttaaccaagcaatagatgaatggattgaagagaacacagacgaa
61  F N Q A I D E W I E E N T D E
29529 caggacagactaattaacttagtcatgaaatggtag 29564
76  Q D R L I N L V M K W *
```

663360 "40B2040

Physico-chemical parameters of ORF 77ORF043

1 MYYEIGEIR KNIHVNGFDF KLFILKGHMG ISIQVKDMNN VPIKHAYVVD ENLDLMASDL
61 FNQAIDEWIE ENTDEQDRLI NLVMKW

Number of amino acids: 86
Average molecular weight (Daltons): 10186.68
Mean amino acid weight (Daltons): 118.45
Monoisotopic molecular weight (Daltons): 10180.02
Mean amino acid monoisotopic weight (Daltons): 118.37

Amino acid composition

Acid	Symbol	Number	%	Average % in Swissprot	Acid	Symbol	Number	%	Average % in Swissprot
Ala	A	3	3.49%	7.58%	Cys	C	0	0.00%	1.66%
Asp	D	9	10.47%	5.28%	Glu	E	7	8.14%	6.37%
Phe	F	4	4.65%	4.09%	Gly	G	4	4.65%	6.84%
His	H	3	3.49%	2.24%	Ile	I	11	12.79%	5.81%
Lys	K	6	6.98%	5.95%	Leu	L	6	6.98%	9.42%
Met	M	5	5.81%	2.37%	Asn	N	8	9.30%	4.45%
Pro	P	1	1.16%	4.9%	Gln	Q	3	3.49%	3.97%
Arg	R	2	2.33%	5.16%	Ser	S	2	2.33%	7.12%
Thr	T	1	1.16%	5.67%	Val	V	6	6.98%	6.58%
Trp	W	2	2.33%	1.23%	Tyr	Y	3	3.49%	3.18%

Number of acidic (negative) amino acids (ED): 16 18.60%
Number of basic (positive) amino acids (KR): 8 9.30%
Total charge (KRED): 24 27.91%
Net charge (KR - ED): -8 -9.30%
Theoretical pI: 4.38
Total linear charge density: 0.30
Average hydrophobicity: -2.80
Ratio of hydrophilicity to hydrophobicity: 1.19
Percentage of hydrophilic amino acid: 48.84%
Percentage of hydrophobic amino acid: 51.16%
Ratio of %hydrophilic to %hydrophobic: 0.95

77ORF102 sequence

```
29051 atgagcaacatttataaaaagctacctagtagcagtattatgcttc
1    M S N I Y K S Y L V A V L C F
29096 acagtcttagcgattgtacttatgccgtttctatacttcactaca
16   T V L A I V L M P F L Y F T T
29141 gcatggtcaattgcgggattcgcaagtatcgcaacattcatgtac
31   A W S I A G F A S I A T F M Y
29186 tacaaagaatgctttttcaaagaataa 29212
46   Y K E C F F K E *
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65360402246

Physico-chemical parameters of ORF 77ORF102

1 MSNIYKSYLV AVLCTVLAI VLMPLYFTT AWSIAGFASI ATFMYYKECF FKE

Number of amino acids: 53
 Average molecular weight (Daltons): 6155.42
 Mean amino acid weight (Daltons): 116.14
 Monoisotopic molecular weight (Daltons): 6151.07
 Mean amino acid monoisotopic weight (Daltons): 116.06

Amino acid composition

Acid	Symbol	Number	%	Average % in Swissprot	Acid	Symbol	Number	%	Average % in Swissprot
Ala	A	6	11.32%	7.58%	Cys	C	2	3.77%	1.66%
Asp	D	0	0.00%	5.28%	Glu	E	2	3.77%	6.37%
Phe	F	7	13.21%	4.09%	Gly	G	1	1.89%	6.84%
His	H	0	0.00%	2.24%	Ile	I	4	7.55%	5.81%
Lys	K	3	5.66%	5.95%	Leu	L	5	9.43%	9.42%
Met	M	3	5.66%	2.37%	Asn	N	1	1.89%	4.45%
Pro	P	1	1.89%	4.9%	Gln	Q	0	0.00%	3.97%
Arg	R	0	0.00%	5.16%	Ser	S	4	7.55%	7.12%
Thr	T	4	7.55%	5.67%	Val	V	4	7.55%	6.58%
Trp	W	1	1.89%	1.23%	Tyr	Y	5	9.43%	3.18%

Number of acidic (negative) amino acids (ED): 2 3.77%
 Number of basic (positive) amino acids (KR): 3 5.66%
 Total charge (KRED): 5 9.43%
 Net charge (KR - ED): 1 1.89%
 Theoretical pI: 8.18
 Total linear charge density: 0.13
 Average hydrophobicity: 10.81
 Ratio of hydrophilicity to hydrophobicity: 0.40
 Percentage of hydrophilic amino acid: 28.30%
 Percentage of hydrophobic amino acid: 71.70%
 Ratio of %hydrophilic to %hydrophobic: 0.39

[illegible]

1144

Physico-chemical parameters of ORF 77ORF104

1 MVTKEFLKTK LECSDMYAQK LIDEAQGDEN RLYDLFIQKL AERHTRPAIV EY

Number of amino acids: 52
 Average molecular weight (Daltons): 6193.13
 Mean amino acid weight (Daltons): 119.10
 Monoisotopic molecular weight (Daltons): 6189.12
 Mean amino acid monoisotopic weight (Daltons): 119.02

Amino acid composition

Acid	Symbol	Number	%	Average % in Swissprot	Acid	Symbol	Number	%	Average % in Swissprot
Ala	A	4	7.69%	7.58%	Cys	C	1	1.92%	1.66%
Asp	D	4	7.69%	5.28%	Glu	E	6	11.54%	6.37%
Phe	F	2	3.85%	4.09%	Gly	G	1	1.92%	6.84%
His	H	1	1.92%	2.24%	Ile	I	3	5.77%	5.81%
Lys	K	5	9.62%	5.95%	Leu	L	6	11.54%	9.42%
Met	M	2	3.85%	2.37%	Asn	N	1	1.92%	4.45%
Pro	P	1	1.92%	4.9%	Gln	Q	3	5.77%	3.97%
Arg	R	3	5.77%	5.16%	Ser	S	1	1.92%	7.12%
Thr	T	3	5.77%	5.67%	Val	V	2	3.85%	6.58%
Trp	W	0	0.00%	1.23%	Tyr	Y	3	5.77%	3.18%

Number of acidic (negative) amino acids (ED): 10 19.23%
 Number of basic (positive) amino acids (KR): 8 15.38%
 Total charge (KRED): 18 34.62%
 Net charge (KR - ED): -2 -3.85%
 Theoretical pI: 5.03
 Total linear charge density: 0.38
 Average hydrophobicity: -5.81
 Ratio of hydrophilicity to hydrophobicity: 1.47
 Percentage of hydrophilic amino acid: 53.85%
 Percentage of hydrophobic amino acid: 46.15%
 Ratio of %hydrophilic to %hydrophobic: 1.17

[illegible]

11

Physico-chemical parameters of ORF 77ORF182

1 MFNIKRKTEE VKMYEIGEI IRKNIHVNGF DFKLFILKGH MGISIQVKDM NNVPIKHAYV
61 VDENDLDMAS DLFNQAIWEV IEENTDEQDR LINLVMKW

Number of amino acids: 98
Average molecular weight (Daltons): 11691.50
Mean amino acid weight (Daltons): 119.30
Monoisotopic molecular weight (Daltons): 11683.84
Mean amino acid monoisotopic weight (Daltons): 119.22

Amino acid composition

Acid	Symbol	Number	%	Average % in Swissprot	Acid	Symbol	Number	%	Average % in Swissprot
Ala	A	3	3.06%	7.58%	Cys	C	0	0.00%	1.66%
Asp	D	9	9.18%	5.28%	Glu	E	9	9.18%	6.37%
Phe	F	5	5.10%	4.09%	Gly	G	4	4.08%	6.84%
His	H	3	3.06%	2.24%	Ile	I	12	12.24%	5.81%
Lys	K	9	9.18%	5.95%	Leu	L	6	6.12%	9.42%
Met	M	6	6.12%	2.37%	Asn	N	9	9.18%	4.45%
Pro	P	1	1.02%	4.9%	Gln	Q	3	3.06%	3.97%
Arg	R	3	3.06%	5.16%	Ser	S	2	2.04%	7.12%
Thr	T	2	2.04%	5.67%	Val	V	7	7.14%	6.58%
Trp	W	2	2.04%	1.23%	Tyr	Y	3	3.06%	3.18%

Number of acidic (negative) amino acids (ED): 18 18.37%
Number of basic (positive) amino acids (KR): 12 12.24%
Total charge (KRED): 30 30.61%
Net charge (KR - ED): -6 -6.12%
Theoretical pI: 4.76
Total linear charge density: 0.33
Average hydrophobicity: -3.89
Ratio of hydrophilicity to hydrophobicity: 1.28
Percentage of hydrophilic amino acid: 51.02%
Percentage of hydrophobic amino acid: 48.98%
Ratio of %hydrophilic to %hydrophobic: 1.04

[illegible]

Query= sid|100017|lan|77ORF017 Phage 77 ORF |23269-23982|-3
(237 letters)

Sequences producing significant alignments:	Score (bits)	E Value
gi 4493986 emb CAB39045.1 (AL034559) predicted using hexExon; ...	41	0.010
gi 730607 sp P23250 RPI1_YEAST NEGATIVE RAS PROTEIN REGULATOR P...	38	0.053
gi 3097044 emb CAA75299 (Y15035) K1R [Cowpox virus]	38	0.090
gi 2146245 pir S73794 hypothetical protein H91_orf180 - Mycopl...	38	0.090
gi 83910 pir S04682 ribosomal protein var1 - yeast (Candida gl...	37	0.15
gi 133135 sp P21358 RMAR_CANGA MITOCHONDRIAL RIBOSOMAL PROTEIN ...	37	0.15
gi 2128843 pir H64475 hypothetical protein MJ1409 - Methanococ...	36	0.20
gi 5107017 gb AAD39926.1 AF126285_2 (AF126285) RNA polymerase [...	36	0.35
gi 2146210 pir S73342 hypothetical protein E07_orf166 - Mycopl...	35	0.60

Sequences producing significant alignments:				Score (bits)	E Value
sp P23250	RPI1_YEAST	NEGATIVE RAS PROTEIN REGULATOR PROTEIN.	38	0.014	
sp P21358	RMAR_CANGA	MITOCHONDRIAL RIBOSOMAL PROTEIN VAR1.	37	0.040	
sp Q21444	LDLC_CAEEL	LDLC PROTEIN HOMOLOG.	34	0.35	
sp P27240	RFAY_ECOLI	LIPOPOLYSACCHARIDE CORE BIOSYNTHESIS PROT...	33	0.46	
sp P53192	YGC0_YEAST	HYPOTHETICAL 27.1 KD PROTEIN IN ALK1-CKB1...	33	0.60	
sp P32908	SMC1_YEAST	CHROMOSOME SEGREGATION PROTEIN SMC1 (DA-B...	33	0.60	
sp P54683	TAGB_DICDI	PRESTALK-SPECIFIC PROTEIN TAGB PRECURSOR ...	32	0.78	
sp Q03100	CYAA_DICDI	ADENYLATE CYCLASE, AGGREGATION SPECIFIC (...)	32	0.78	

BLASTP 2.0.8 [Jan-05-1999]

Query= sid|100019|lan|77ORF019 Phage 77 ORF|39851-40501|2
(216 letters)

Database: nr
373,355 sequences; 114,214,446 total letters

Sequences producing significant alignments:	Score	E
Value	(bits)	
gi 3341966 dbj BAA31932 (AB009866) orf 59 [bacteriophage phi PVL]	437	e-122
gi 2689911 (AE000792) B. burgdorferi predicted coding region BB...	38	0.058
gi 1171589 emb CAA64574 (X95275) frameshift [Plasmodium falcip...	37	0.10
gi 4493986 emb CAB39045.1 (AL034559) predicted using hexExon; ...	36	0.23
gi 141257 sp P18019 YPI9_CLOPE HYPOTHETICAL 14.5 KD PROTEIN (OR...	36	0.29
gi 133412 sp P27059 RPOB_ASTLO DNA-DIRECTED RNA POLYMERASE BETA...	35	0.51
gi 3122231 sp Q58851 HISX_METJA HISTIDINOL DEHYDROGENASE (HDH) ...	35	0.51
gi 3649757 emb CAB11106.1 (Z98547) predicted using hexExon; MA...	34	0.66
gi 2688313 (AE001146) sensory transduction histidine kinase, pu...	34	0.87

Database: swissprot
79,449 sequences; 28,874,452 total letters

Sequences producing significant alignments:	Score	E
Value	(bits)	
sp P18019 YPI9_CLOPE HYPOTHETICAL 14.5 KD PROTEIN (ORF9).	36	0.079
sp Q58851 HISX_METJA HISTIDINOL DEHYDROGENASE (EC 1.1.1.23) (H...	35	0.14
sp P27059 RPOB_ASTLO DNA-DIRECTED RNA POLYMERASE BETA CHAIN (E...	35	0.14
sp Q02224 CENE_HUMAN CENTROMERIC PROTEIN E (CENP-E PROTEIN).	34	0.31
sp P04931 ARP_PLAFA ASPARAGINE-RICH PROTEIN (AG319) (ARP) (FRA...	33	0.53
sp P18011 IPAB_SHIFL 62 KD MEMBRANE ANTIGEN.	32	0.69
sp P18709 VTA2_XENLA VITELLOGENIN A2 PRECURSOR (VTG A2) [CONTA...	32	0.90
sp Q64409 CP3H_CAVPO CYTOCHROME P450 3A17 (EC 1.14.14.1) (CYPI...	32	0.90
sp P21358 RMAR_CANGA MITOCHONDRIAL RIBOSOMAL PROTEIN VAR1.	32	0.90
sp Q03945 IPAB_SHIDY 62 KD MEMBRANE ANTIGEN.	32	1.2

BLASTP 2.0.8 [Jan-05-1999]

Query= sid|100043|lan|77ORF043 Phage 77 ORF|29304-29564|3
(86 letters)

Database: nr
373,355 sequences; 114,214,446 total letters

Sequences producing significant alignments:	Score (bits)	E Value
gi 3341947 dbj BAA31913 (AB009866) orf 39 [bacteriophage phi PVL]	182	6e-46
gi 744518 prf 2014422A FKBP-rapamycin-associated protein [Homo...	32	0.84
gi 1169736 sp P42346 FRAP_RAT FKBP-RAPAMYCIN ASSOCIATED PROTEIN...	32	0.84
gi 1169735 sp P42345 FRAP_HUMAN FKBP-RAPAMYCIN ASSOCIATED PROTE...	32	0.84
gi 3282239 (U88966) rapamycin associated protein FRAP2 [Homo sa...	32	0.84
gi 3875402 emb CAA98122 (Z73906) cDNA EST EMBL:D64544 comes fr...	31	2.5
gi 1084792 pir S54091 hypothetical protein YPR070w - yeast (Sa...	30	4.2

Database: swissprot
79,449 sequences; 28,874,452 total letters

Sequences producing significant alignments:	Score (bits)	E Value
sp P42345 FRAP_HUMAN FKBP-RAPAMYCIN ASSOCIATED PROTEIN (FRAP) ...	32	0.24
sp P42346 FRAP_RAT FKBP-RAPAMYCIN ASSOCIATED PROTEIN (FRAP) (R...	32	0.24
sp P34554 YNP1_CAEEL HYPOTHETICAL 42.2 KD PROTEIN T05G5.1 IN C...	28	3.5
sp Q24118 LIO_DROME LINOTTE PROTEIN.	28	3.5
sp P80034 ACH2_BOMMO ANTICHYMOTRYPSIN II (ACHY-II).	28	3.5
sp P22922 A1AT_BOMMO ANTITRYPSIN PRECURSOR (AT).	28	3.5
sp Q44363 TRAA_AGRT6 CONJUGAL TRANSFER PROTEIN TRAA.	28	3.5
sp P38255 YBU5_YEAST HYPOTHETICAL 51.3 KD PROTEIN IN PHO5-VPS1...	27	6.0
sp P55822 SH3B_HUMAN SH3BGR PROTEIN (21-GLUTAMIC ACID-RICH PRO...	27	7.9
sp Q58482 YA82_METJA HYPOTHETICAL PROTEIN MJ1082.	27	7.9
sp P34252 YKK8_YEAST HYPOTHETICAL 52.3 KD PROTEIN IN HAP4-AAT1...	27	7.9

Species	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	

Sequences producing significant alignments:	Score (bits)	E Value
sp P42087 HUTM_BACSU PUTATIVE HISTIDINE PERMEASE.	26	7.1
sp P04775 CIN2_RAT SODIUM CHANNEL PROTEIN, BRAIN II ALPHA SUBU...	26	9.2
sp P42619 YQJF_ECOLI HYPOTHETICAL 17.2 KD PROTEIN IN EXUR-TDCC...	26	9.2

[illegible]

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BLASTP 2.0.8 [Jan-05-1999]

Query= sid|122748|lan|77ORF182 Phage 77 ORF|29268-29564|3
(98 letters)

Database: nr
393,678 sequences; 120,452,765 total letters

	Score (bits)	E Value
Sequences producing significant alignments:		
gi 3341947 dbj BAA31913.1 (AB009866) orf 39 [bacteriophage phi...	182	8e-46
gi 1084792 pir S54091 hypothetical protein YPR070w - yeast (Sa...	35	0.13
gi 1169736 sp P42346 FRAP_RAT FKBP-RAPAMYCIN ASSOCIATED PROTEIN...	32	1.1
gi 744518 prf 2014422A FKBP-rapamycin-associated protein [Homo...	32	1.1
gi 5051381 emb CAB44736.1 (AL049653) dJ647M16.2 (FK506 binding...	32	1.1
gi 4826730 ref NP_004949.1 pFRAP1 FK506 binding protein 12-rap...	32	1.1
gi 3282239 (U88966) rapamycin associated protein FRAP2 [Homo sa...	32	1.1

Database: swissprot
79,909 sequences; 29,054,478 total letters

	Score (bits)	E Value
Sequences producing significant alignments:		
sp P42345 FRAP_HUMAN FKBP-RAPAMYCIN ASSOCIATED PROTEIN (FRAP) ...	32	0.29
sp P42346 FRAP_RAT FKBP-RAPAMYCIN ASSOCIATED PROTEIN (FRAP) (R...	32	0.29
sp P40557 YIA5_YEAST PUTATIVE DISULFIDE ISOMERASE YIL005W PREC...	29	3.3
sp Q24118 LIO_DROME LINOTTE PROTEIN.	28	4.4
sp Q44363 TRAA_AGRT6 CONJUGAL TRANSFER PROTEIN TRAA.	28	4.4
sp P80034 ACH2_BOMMO ANTICHYMOTRYPSIN II (ACHY-II).	28	4.4
sp P34554 YNP1_CAEEL HYPOTHETICAL 42.2 KD PROTEIN T05G5.1 IN C...	28	4.4
sp P22922 A1AT_BOMMO ANTITRYPSIN PRECURSOR (AT).	28	4.4

List of phage 77 ORFs that were functionally tested

Table 5

1	77ORF005	48	77ORF052
2	77ORF006	49	77ORF053
3	77ORF007	50	77ORF054
4	77ORF008	51	77ORF055
5	77ORF009	52	77ORF058
6	77ORF010	53	77ORF059
7	77ORF011	54	77ORF064
8	77ORF012	55	77ORF065
9	77ORF013	56	77ORF066
10	77ORF014	57	77ORF069
11	77ORF015	58	77ORF070
12	77ORF016	59	77ORF071
13	77ORF017	60	77ORF072
14	77ORF018	61	77ORF073
15	77ORF019	62	77ORF074
16	77ORF020	63	77ORF075
17	77ORF021	64	77ORF077
18	77ORF022	65	77ORF079
19	77ORF023	66	77ORF080
20	77ORF024	67	77ORF085
21	77ORF025	68	77ORF092
22	77ORF026	69	77ORF094
23	77ORF027	70	77ORF096
24	77ORF028	71	77ORF098
25	77ORF029	72	77ORF102
26	77ORF030	73	77ORF104
27	77ORF031	74	77ORF109
28	77ORF032	75	77ORF112
29	77ORF033	76	77ORF117
30	77ORF034	77	77ORF118
31	77ORF035	78	77ORF120
32	77ORF036	79	77ORF124
33	77ORF037	80	77ORF128
34	77ORF038	81	77ORF130
35	77ORF039	82	77ORF133
36	77ORF040	83	77ORF140
37	77ORF041	84	77ORF147
38	77ORF042	85	77ORF149
39	77ORF043	86	77ORF151
40	77ORF044	87	77ORF155
41	77ORF045	88	77ORF157
42	77ORF046	89	77ORF167
43	77ORF047	90	77ORF175
44	77ORF048	91	77ORF176
45	77ORF049	92	77ORF178
46	77ORF050	93	77ORF179
47	77ORF051		

Table 6

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- ☐ U77328
Staphylococcus aureus staphylokinase gene, partial cds
gi|2605637|gb|U77328.1|SAU77328 [2605637]
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- ☐ AF151117
Staphylococcus aureus plasmid pKH3, complete sequence
gi|5031412|gb|AF151117.1|AF151117 [5031412]
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- ☐ AF151218
Staphylococcus aureus ribonuclease P RNA gene, complete sequence
gi|4929536|gb|AF151218.1|AF151218 [4929536]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), or [Graphical view](#))
- ☐ AF146368
Staphylococcus aureus 16S ribosomal RNA gene, partial sequence
gi|4929362|gb|AF146368.1|AF146368 [4929362]
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- ☐ AF144661
Staphylococcus aureus subsp. anaerobius factor essential for methicillin resistance (femA) gene, complete cds
gi|4929298|gb|AF144661.1|AF144661 [4929298]
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- ☐ AF132117
Staphylococcus aureus ferrichrome uptake operon, complete sequence and unknown genes
gi|4928288|gb|AF132117.1|AF132117 [4928288]
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- ☐ Y15477
Staphylococcus aureus argI, glmM genes and ORF1 and ORF2
gi|3892891|emb|Y15477.1|SAARGFEMD [3892891]
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- ☐ Y09928
S.aureus CTORF1365, partial
gi|4775550|emb|Y09928.1|SACTORF13 [4775550]
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- ☐ Y09594
S.aureus arg gene
gi|4775541|emb|Y09594.1|SAARG [4775541]
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- ☐ AF134905
Staphylococcus aureus plasmid pRW001 CadD (cadD) gene, complete cds
gi|4680369|gb|AF134905.1|AF134905 [4680369]
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- ☐ AB019536
Staphylococcus aureus norA23 gene for NorA, complete cds
gi|4115706|dbj|AB019536.1|AB019536 [4115706]
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- ☐ AJ237696
Staphylococcus aureus fus gene
gi|4582215|emb|AJ237696.1|SAU237696 [4582215]
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- ☐ AF106851
Staphylococcus aureus LytN (lytN) and FmhC (fmhC) genes, complete cds
gi|4574236|gb|AF106851.1|AF106851 [4574236]
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- ☐ AF106850
Staphylococcus aureus FmhB (fmhB) gene, complete cds
gi|4574234|gb|AF106850.1|AF106850 [4574234]
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- ☐ AF106849
Staphylococcus aureus FmhA (fmhA) gene, complete cds
gi|4574232|gb|AF106849.1|AF106849 [4574232]
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- ☐ M26321
Staphylococcus aureus plasmid pT181 repC gene, partial cds
gi|151689|gb|M26321.1|PT1REPC [151689]
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- ☐ AF060191
Staphylococcus aureus strain ATCC27664 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558749|gb|AF060191.1|AF060191 [4558749]
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- ☐ AF060190
Staphylococcus aureus strain ATCC19095 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558747|gb|AF060190.1|AF060190 [4558747]
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- ☐ AF060189
Staphylococcus aureus strain ATCC14458 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558745|gb|AF060189.1|AF060189 [4558745]
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- ☐ AF060188
Staphylococcus aureus strain ATCC13565 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558743|gb|AF060188.1|AF060188 [4558743]
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- ☐ AF060187
Staphylococcus aureus strain ATCC10832 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558741|gb|AF060187.1|AF060187 [4558741]
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- ☐ AF060186
Staphylococcus aureus strain ATCC12598 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558739|gb|AF060186.1|AF060186 [4558739]
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- ☐ AF060185
Staphylococcus aureus strain ATCC25178 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558737|gb|AF060185.1|AF060185 [4558737]
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- ☐ AF060184
Staphylococcus aureus strain ATCC27217 heat shock protein 60 kDa (hsp60) gene, partial cds
gi|4558735|gb|AF060184.1|AF060184 [4558735]
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- ☐ AF036324
Staphylococcus aureus subsp. aureus heat shock protein 60 (GroEL) gene, partial cds
gi|4558705|gb|AF036324.1| [4558705]
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- ☐ AF036323
Staphylococcus aureus subsp. anaerobius heat shock protein 60 (GroEL) gene, partial cds
gi|4558703|gb|AF036323.1|AF036323 [4558703]
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- ☐ AF053568
Staphylococcus aureus ATCC 25923 heat shock protein 60 gene, partial cds
gi|4205742|gb|AF053568.1|AF053568 [4205742]
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- ☐ AJ132841
Staphylococcus aureus mapN gene
gi|4454323|emb|AJ132841.1|SAU132841 [4454323]
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- ☐ Y13766
Staphylococcus aureus pnpA gene
gi|3970796|emb|Y13766.1|SAPNPA [3970796]
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- ☐ AF101234
Staphylococcus aureus dltABCD operon, complete sequence; and unknown gene
gi|4530239|gb|AF101234.1|AF101234 [4530239]
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- ☐ AJ133520
Staphylococcus aureus gap operon (gapR, gap, pgk and tpi genes)
gi|4490611|emb|AJ133520.1|SAU133520 [4490611]
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- ☐ AJ133495
Staphylococcus aureus ribonucleotide reductase operon
gi|4490607|emb|AJ133495.1|SAU133495 [4490607]
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- ☐ AJ132803
Staphylococcus aureus ORF1 and ORF2 (partial)

gi|4454320|emb|AJ132803.1|SAU132803 [4454320]
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- ☐ AB016487
Staphylococcus aureus gene for enterotoxin type Gv, complete cds
gi|4126682|dbj|AB016487.1|AB016487 [4126682]
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- ☐ AB016431
Staphylococcus aureus, zinc responsible operon czr genes, complete and partial cds
gi|4126670|dbj|AB016431.1|AB016431 [4126670]
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- ☐ AB015981
Staphylococcus aureus genes for OrfA, MnhA, MnhB, MnhC, MnhD, MnhE, MnhF and MnhG, complete cds
gi|4001723|dbj|AB015981.1|AB015981 [4001723]
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- ☐ AB015195
Staphylococcus aureus gene for LytN and Ephr, complete cds
gi|3767591|dbj|AB015195.1|AB015195 [3767591]
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- ☐ AF107307
Staphylococcus aureus subsp. anaerobius 16S ribosomal RNA gene, partial sequence
gi|4406286|gb|AF107307.1|AF107307 [4406286]
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- ☐ AF079518
Staphylococcus aureus lipoprotein SirA (sirA), SirB (sirB), and SirC (sirC) genes, complete cds
gi|3694941|gb|AF079518.1|AF079518 [3694941]
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- ☐ AJ223806
Staphylococcus aureus map gene, partial
gi|4138455|emb|AJ223806.1|SAU223806 [4138455]
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- ☐ Y18018
Staphylococcus aureus plasmid pSES30 including ermC gene, partial
gi|4138444|emb|Y18018.1|SAU18018 [4138444]
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- ☐ Y17795
Staphylococcus aureus prfA, pbp2 genes
gi|3955029|emb|Y17795.1|SAU17795 [3955029]
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- ☐ AJ005647
Staphylococcus aureus sdrE gene
gi|3550595|emb|AJ005647.1|SAU5647 [3550595]
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- ☐ AJ005646
Staphylococcus aureus sdrD gene
gi|3550593|emb|AJ005646.1|SAU5646 [3550593]
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- ☐ AJ005645
Staphylococcus aureus sdrC gene
gi|3550591|emb|AJ005645.1|SAU5645 [3550591]
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- ☐ V01282
Staphylococcus aureus plasmid pSN2 Includes an unknown gene
gi|46653|emb|V01282.1|SAPSN2 [46653]
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- ☐ AF121672
Staphylococcus aureus superoxide dismutase SodA (sodA) gene, complete cds
gi|4325246|gb|AF121672.1|AF121672 [4325246]
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- ☐ AF072726
Staphylococcus aureus putative heme A synthase (ctaA) gene, complete cds
gi|3320605|gb|AF072726.1|AF072726 [3320605]
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- ☐ AF115379
Staphylococcus aureus surface protein Pls (pls) gene, complete cds
gi|4185564|gb|AF115379.1|AF115379 [4185564]
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- ☐ AF034153
Staphylococcus aureus phospho-N-acetylmuramoyl-pentapeptide translocase (mraY) gene,

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- ☐ AF029244
Staphylococcus aureus 60 kDa heat shock protein (hsp60) gene, partial cds
gi|4103899|gb|AF029244.1|AF029244 [4103899]
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- ☐ U67965
Staphylococcus aureus lytic regulatory protein gene, complete cds
gi|4097756|gb|U67965.1|SAU67965 [4097756]
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- ☐ U96610
Staphylococcus aureus plasmid pSK6, complete genome
gi|4090653|gb|U96610.1|SAU96610 [4090653]
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- ☐ U96609
Staphylococcus aureus plasmid pSK3, complete genome
gi|4090650|gb|U96609.1|SAU96609 [4090650]
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- ☐ U73027
Staphylococcus aureus transposon Tn5405 unknown gene, complete cds
gi|2811117|gb|U73027.1|SAU73027 [2811117]
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- ☐ U73026
Staphylococcus aureus transposon Tn5405 streptothricine-acetyl-transferase (sat4) pseudogene, complete sequence
gi|2811116|gb|U73026.1|SAU73026 [2811116]
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- ☐ U73025

Staphylococcus aureus transposon Tn5405 unknown gene, complete cds

gi|2811114|gb|U73025.1|SAU73025 [2811114]

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☐ AF068904

Staphylococcus aureus cell division protein FtsZ (ftsZ) gene, partial cds; YlmD (ylmD), YlmE (ylmE), YlmF (ylmF), YlmG (ylmG), and YlmH (ylmH) genes, complete cds; and cell division protein DivIVA (divIVA) gene, partial cds

gi|4009490|gb|AF068904.1|AF068904 [4009490]

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☐ U60050

Staphylococcus aureus major cold-shock protein (cspA) gene, partial cds

gi|1402770|gb|U60050.1|SAU60050 [1402770]

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☐ D10907

Staphylococcus aureus insertion element IS431, partial sequence, clone:MR108-4

gi|216973|dbj|D10907.1|STAIS431B [216973]

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☐ D10906

Staphylococcus aureus insertion element IS431, partial sequence, clone:MR108-3

gi|216972|dbj|D10906.1|STAIS431A [216972]

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☐ AF053140

Staphylococcus aureus plasmid pIB485 enterotoxin D (sed) gene, partial cds; and enterotoxin J (sej) gene, complete cds

gi|3372540|gb|AF053140.1|AF053140 [3372540]

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☐ AB013298

Staphylococcus aureus genes for leader peptide, MsrSA and MphBM, complete cds

gi|3892641|dbj|AB013298.1|AB013298 [3892641]

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☐ Y16431

Staphylococcus aureus dpj, alr genes, partial kdpC gene and 4 ORF's

gi|3850845|emb|Y16431.1|SAU16431 [3850845]

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☐ AF076684

Staphylococcus aureus oligopeptide transporter putative membrane permease domain (opp-2B), oligopeptide transporter putative membrane permease domain (opp-2C), oligopeptide transporter putative ATPase domain (opp-2D), and oligopeptide transporter putative ATPase domain (opp-2F) genes, complete cds

gi|3800824|gb|AF076684.1|AF076684 [3800824]

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☐ AF076683

Staphylococcus aureus oligopeptide transporter putative substrate binding domain (opp-1A), oligopeptide transporter putative membrane permease domain (opp-1B), oligopeptide transporter putative membrane permease domain (opp-1C), oligopeptide transporter putative ATPase domain (opp-1D), and oligopeptide transporter putative ATPase domain (opp-1F) genes, complete cds; and unknown gene

gi|3800817|gb|AF076683.1|AF076683 [3800817]

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☐ Y13225

Staphylococcus aureus lukE, lukD genes

gi|2765302|emb|Y13225.1|SALUKED [2765302]

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☐ AF094826

Staphylococcus aureus novel exotoxins gene cluster, complete sequence; and HsdM-like protein gene, partial cds

gi|3806103|gb|AF094826.1|AF094826 [3806103]

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☐ AJ223480

Staphylococcus aureus trxA and uvrC genes and partial mutS and dhsC genes

gi|3776109|emb|AJ223480.1|SATRXA [3776109]

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☐ AF093548

Staphylococcus aureus tyrosine recombinase XerD (xerD) gene, complete cds

gi|3747041|gb|AF093548.1|AF093548 [3747041]

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☐ AJ005352

Staphylococcus aureus, Sst putative iron transport operon

gi|3724154|emb|AJ005352.1|SAA005352 [3724154]

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☐ AF051916

Staphylococcus aureus plasmid pJE1 remnant of replication protein Rep (rep), trimethoprim resistance protein DfrA (dfrA), thymidylate synthetase ThyE (thyE), and putative transposase Tnp (tnp) genes, complete cds; and unknown gene

gi|3676404|gb|AF051916.1|AF051916 [3676404]

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protein links, or 22 nucleotide neighbors)

☐ Y09927

S.aureus glmM gene

gi|1729788|emb|Y09927.1|SAURED [1729788]

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☐ AF051917

Staphylococcus aureus plasmid pSK41, complete sequence

gi|3676412|gb|AF051917.1|AF051917 [3676412]

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☐ S77058

bler=bleomycin-resistance gene [Staphylococcus aureus, MRSA, B-26, Genomic, 297 nt]

gi|913952|gb|S77058.1|S77058 [913952]

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☐ S65052

hlg2=gamma-hemolysin II...lukF=leukocidin F component [Staphylococcus aureus, MRSA No. 4, Genomic, 3 genes, 4353 nt]

gi|410004|gb|S65052.1|S65052 [410004]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 MEDLINE link, 3 protein links, or 2 nucleotide neighbors)

☐ AF009671

Staphylococcus aureus UDP-N-acetylmuramoyl-L-alanine : D-glutamate ligase (murD) gene, complete cds

gi|2305091|gb|AF009671.1|AF009671 [2305091]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 MEDLINE link, or 1 protein link)

☐ U81973

Staphylococcus aureus capsule gene cluster Cap5A through Cap5P genes, complete cds

gi|1773339|gb|U81973.1|SAU81973 [1773339]

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☐ U77308

Staphylococcus aureus O-acetyl transferase (cap5H) gene, complete cds

gi|1673628|gb|U77308.1|SAU77308 [1673628]

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☐ U20869

Staphylococcus aureus ribosomal protein S12 (rpsL) gene, complete cds, ribosomal protein S7 (rpsG) and ORF 1 genes, partial cds

gi|706919|gb|U20869.1|SAU20869 [706919]

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protein links, or 2 nucleotide neighbors)

☐ U89396

Staphylococcus aureus hemCDBL gene cluster: porphobilinogen deaminase (hemC), uroporphyrinogen III synthase (hemD), d-aminolevulinic acid dehydratase (hemB) and GSA-1-aminotransferase (hemL) genes, complete cds

gi|2589180|gb|U89396.1|SAU89396 [2589180]

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☐ U94706

Staphylococcus aureus strain ATCC 8325-4 cell wall/cell division gene cluster, yllB, yllC, yllD, pbpA, mraY, murD, div1B, ftsA and ftsZ genes, complete cds

gi|2149889|gb|U94706.1|SAU94706 [2149889]

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☐ U41072

Staphylococcus aureus isoleucyl-tRNA synthetase (ileS) gene, partial cds

gi|1314300|gb|U41072.1|SAU41072 [1314300]

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☐ U52961

Staphylococcus aureus holin-like protein LrgA (lrgA) and LrgB (lrgB) genes, complete cds

gi|1841516|gb|U52961.1|SAU52961 [1841516]

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☐ U21636

Staphylococcus aureus cmp-binding-factor 1 (cbf1) and ORF X genes, complete cds

gi|710420|gb|U21636.1|SAU21636 [710420]

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☐ U65000

Staphylococcus aureus type-I signal peptidase SpsA (spsA) gene, and type-I signal peptidase SpsB (spsB) gene, complete cds

gi|1595808|gb|U65000.1|SAU65000 [1595808]

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☐ U48826

Staphylococcus aureus elastin binding protein (ebpS) gene, complete cds

gi|1397238|gb|U48826.1|SAU48826 [1397238]

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☐ U20503

Staphylococcus aureus MHC class II analog gene, complete cds

gi|1001960|gb|U20503.1|SAU20503 [1001960]

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- ☐ U11789
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV8 16S-23S rRNA spacer region
gi|644560|gb|U11789.1|SAU11789 [644560]
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- ☐ U11788
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV7 16S-23S rRNA spacer region
gi|644559|gb|U11788.1|SAU11788 [644559]
([View GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [1 MEDLINE link](#), or [386 nucleotide neighbors](#))
- ☐ U11787
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV43 16S-23S rRNA spacer region
gi|644558|gb|U11787.1|SAU11787 [644558]
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- ☐ U11786
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV42 16S-23S rRNA spacer region
gi|644557|gb|U11786.1|SAU11786 [644557]
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- ☐ U11785
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV41 16S-23S rRNA spacer region
gi|644556|gb|U11785.1|SAU11785 [644556]
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- ☐ U11784
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV40 16S-23S rRNA spacer region
gi|644555|gb|U11784.1|SAU11784 [644555]
([View GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [1 MEDLINE link](#), or [1780 nucleotide neighbors](#))
- ☐ U11783
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV4 16S-23S rRNA spacer region
gi|644554|gb|U11783.1|SAU11783 [644554]
([View GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [1 MEDLINE link](#), or [1737 nucleotide neighbors](#))

- ☐ U11782
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV38 16S-23S rRNA
spacer region
gi|644553|gb|U11782.1|SAU11782 [644553]
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- ☐ U11781
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV34 16S-23S rRNA
spacer region
gi|644552|gb|U11781.1|SAU11781 [644552]
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- ☐ U11780
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV32 16S-23S rRNA
spacer region
gi|644551|gb|U11780.1|SAU11780 [644551]
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- ☐ U11779
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV30 16S-23S rRNA
spacer region
gi|644550|gb|U11779.1|SAU11779 [644550]
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- ☐ U11778
Staphylococcus aureus methicillin-resistant ATCC 33952 clone RRNV27 16S-23S rRNA
spacer region
gi|644549|gb|U11778.1|SAU11778 [644549]
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- ☐ U11777
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV2 16S-23S rRNA spacer region
gi|644548|gb|U11777.1|SAU11777 [644548]
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- ☐ U11776
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV17 16S-23S rRNA spacer region
gi|644547|gb|U11776.1|SAU11776 [644547]
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- ☐ U11775
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV13 16S-23S rRNA spacer region
gi|644546|gb|U11775.1|SAU11775 [644546]
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- ☐ U11774
Staphylococcus aureus methicillin-resistant isolate H11 clone RRNV12 16S-23S rRNA spacer region
gi|644545|gb|U11774.1|SAU11774 [644545]
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- ☐ U11773
Staphylococcus aureus methicillin-resistant isolate D46 clone RRN4 16S-23S rRNA spacer region
gi|644544|gb|U11773.1|SAU11773 [644544]
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- ☐ AF053772
Staphylococcus aureus plasmid pSK23 putative recombinase Sin (sin) gene, partial cds; and transcriptional regulator QacR (qacR) and multidrug efflux protein QacB (qacB) genes, complete cds

gi|3327946|gb|AF053772.1|AF053772 [3327946]
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☐ AF053771

Staphylococcus aureus plasmid pSK156 transcriptional regulator QacR (qacR), multidrug efflux protein QacB, delta-orf186, and putative transposase TnpA (tnpA) genes, complete cds
gi|3327941|gb|AF053771.1|AF053771 [3327941]
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☐ AF029731

Staphylococcus aureus large conductance mechanosensitive channel (mscL) gene, complete cds
gi|3135291|gb|AF029731.1|AF029731 [3135291]
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☐ AF027155

Staphylococcus aureus IgG-binding protein SBI (sbi) gene, complete cds
gi|2827911|gb|AF027155.1|AF027155 [2827911]
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☐ AF024571

Staphylococcus aureus high affinity proline permease (putP) gene, complete cds
gi|2565310|gb|AF024571.1|AF024571 [2565310]
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☐ U87144

Staphylococcus aureus branched-chain amino acid carrier protein gene, complete cds
gi|2315994|gb|U87144.1|SAU87144 [2315994]
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☐ AF086644

Staphylococcus aureus type b beta-lactamase (blaZ) gene, partial cds
gi|3603440|gb|AF086644.1|AF086644 [3603440]
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☐ AJ223781

Staphylococcus aureus trxB gene
gi|4379427|emb|AJ223781.1|SAAJ3781 [4379427]
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☐ AF076030

Staphylococcus aureus 16S ribosomal RNA gene, partial sequence
gi|3551854|gb|AF076030.1|AF076030 [3551854]
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neighbors)

- ☐ AF044951
Staphylococcus aureus repressor protein (rzcA) and transport protein (rzcB) genes, complete cds
gi|3445565|gb|AF044951.1|AF044951 [3445565]
(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 MEDLINE link, or 2 protein links)
- ☐ AF044906
Staphylococcus aureus isolate SA92 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411113|gb|AF044906.1|AF044906 [3411113]
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- ☐ AF044905
Staphylococcus aureus isolate SA32 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411111|gb|AF044905.1|AF044905 [3411111]
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- ☐ AF044904
Staphylococcus aureus isolate SA22 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411109|gb|AF044904.1|AF044904 [3411109]
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- ☐ AF044903
Staphylococcus aureus isolate SA198 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411107|gb|AF044903.1|AF044903 [3411107]
(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 MEDLINE link, 1 protein link, or 55 nucleotide neighbors)
- ☐ AF044902
Staphylococcus aureus isolate SA85 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411105|gb|AF044902.1|AF044902 [3411105]
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- ☐ AF044901
Staphylococcus aureus isolate SA76 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411103|gb|AF044901.1|AF044901 [3411103]
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- ☐ AF044900
Staphylococcus aureus isolate SA75 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411101|gb|AF044900.1|AF044900 [3411101]
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- ☐ AF044899
Staphylococcus aureus isolate R155 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411099|gb|AF044899.1|AF044899 [3411099]
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- ☐ AF044898
Staphylococcus aureus isolate SAM1 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411097|gb|AF044898.1|AF044898 [3411097]
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- ☐ AF044897
Staphylococcus aureus isolate SA74 DNA topoisomerase IV subunit A (grlA) gene, partial cds
gi|3411095|gb|AF044897.1|AF044897 [3411095]
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- ☐ AF044075
Staphylococcus aureus isolate sa92 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411091|gb|AF044075.1|AF044075 [3411091]
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- ☐ AF044074
Staphylococcus aureus isolate sa32 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411089|gb|AF044074.1|AF044074 [3411089]
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- ☐ AF044073
Staphylococcus aureus isolate sa22 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411087|gb|AF044073.1|AF044073 [3411087]
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- ☐ AF044072
Staphylococcus aureus isolate sa198 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411085|gb|AF044072.1|AF044072 [3411085]
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- ☐ AF044071
Staphylococcus aureus isolate sa85 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411083|gb|AF044071.1|AF044071 [3411083]
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- ☐ AF044070
Staphylococcus aureus isolate sa76 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411081|gb|AF044070.1|AF044070 [3411081]
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- ☐ AF044069
Staphylococcus aureus isolate sa75 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411079|gb|AF044069.1|AF044069 [3411079]
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- ☐ AF044068
Staphylococcus aureus isolate R155 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411077|gb|AF044068.1|AF044068 [3411077]
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- ☐ AF044067
Staphylococcus aureus isolate SAM1 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411075|gb|AF044067.1|AF044067 [3411075]
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- ☐ AF044066
Staphylococcus aureus isolate sa74 DNA gyrase subunit A (gyrA) gene, partial cds
gi|3411073|gb|AF044066.1|AF044066 [3411073]
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- ☐ U93688
Staphylococcus aureus toxic shock syndrome toxin-1 (tst), enterotoxin (ent), and integrase (int) genes, complete cds
gi|2689547|gb|U93688.1|U93688 [2689547]
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- ☐ U93687
Staphylococcus aureus attachment site for Tn557
gi|2689546|gb|U93687.1|U93687 [2689546]
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- ☐ AJ224764
Staphylococcus aureus strain Newman clumping factor B (clfB) gene
gi|3393010|emb|AJ224764.1|SAA224764 [3393010]
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- ☐ AF064774
Staphylococcus aureus extracellular enterotoxin type I precursor (SEI) gene, complete cds

gi|3323612|gb|AF064774.1|AF064774 [3323612]
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☐ AF064773
Staphylococcus aureus extracellular enterotoxin type G precursor (SEG) gene, complete cds
gi|3323610|gb|AF064773.1|AF064773 [3323610]
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☐ Y14370
Staphylococcus aureus RF3, murE, ypfP genes
gi|3256221|emb|Y14370.1|SAY14370 [3256221]
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☐ AF065394
Staphylococcus aureus enolase (eno) gene, complete cds
gi|3152724|gb|AF065394.1|AF065394 [3152724]
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☐ AF062376
Staphylococcus aureus strain E3452, unidentified sequence 2
gi|3142435|gb|AF062376.1|AF062376 [3142435]
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☐ AF062375
Staphylococcus aureus strain E3452, unidentified sequence 1
gi|3142434|gb|AF062375.1|AF062375 [3142434]
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☐ AF062374
Staphylococcus aureus strain W6652, unidentified sequence 2
gi|3142433|gb|AF062374.1|AF062374 [3142433]
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☐ AF062373
Staphylococcus aureus strain W6652, unidentified sequence 1
gi|3142432|gb|AF062373.1|AF062373 [3142432]
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☐ AB007500
Staphylococcus aureus genes for penicillin-binding protein 1, MraY, MurD, partial and complete cds
gi|2463558|dbj|AB007500.1|AB007500 [2463558]
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☐ Y09924

S.aureus serS gene

gi|1835217|emb|Y09924.1|SASERS [1835217]

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☐ U63529

Staphylococcus aureus novel antigen gene, complete cds

gi|1488694|gb|U63529.1|SAU63529 [1488694]

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☐ AF033191

Staphylococcus aureus strain ATCC25923 clone pSa-442 Sau3AI fragment

gi|2988485|gb|AF033191.1|AF033191 [2988485]

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- ☐ Y15856
Staphylococcus aureus 16S rRNA gene
gi|2950318|emb|Y15856.1|SAY15856 [2950318]
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- ☐ AB000439
Staphylococcus aureus recG gene, complete cds
gi|2826895|dbj|AB000439.1|AB000439 [2826895]
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- ☐ AF041467
Staphylococcus aureus coenzyme A disulfide reductase gene, complete cds
gi|2792489|gb|AF041467.1|AF041467 [2792489]
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- ☐ Y14051
Staphylococcus aureus mecA, mecR1, mecI genes and ORF168, ORF142, ORF44, ORF145 and ORF224
gi|2791983|emb|Y14051.1|SAMECAR1I [2791983]
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- ☐ U82085
Staphylococcus aureus plasmid pIP1633 pristinamycin resistance protein VgaB (vgaB) gene, complete cds
gi|2769707|gb|U82085.1|SAU82085 [2769707]
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- ☐ AF026122
Staphylococcus aureus plasmid pIM51 signal transduction protein (agrB) gene, partial cds; pre-pheromone (agrD) and mutant sensor protein (agrC) genes, complete cds; and transducer protein (agrA) gene, partial cds
gi|2736224|gb|AF026122.1|AF026122 [2736224]
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- ☐ AF026121
Staphylococcus aureus plasmid pIM50 signal transduction protein (agrB) gene, partial cds; pre-pheromone (agrD) and mutant sensor protein (agrC) genes, complete cds; and transducer protein (agrA) gene, partial cds
gi|2736219|gb|AF026121.1|AF026121 [2736219]
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- ☐ AF026120
Staphylococcus aureus plasmid pIM49 signal transduction protein (agrB) gene, partial cds; pre-pheromone (agrD) and mutant sensor protein (agrC) genes, complete cds; and transducer protein (agrA) gene, partial cds
gi|2736214|gb|AF026120.1|AF026120 [2736214]
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- ☐ AB009635
Staphylococcus aureus DNA for Fmt, complete cds
gi|2696795|dbj|AB009635.1|AB009635 [2696795]
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- ☐ AB006796
Staphylococcus aureus genes for LukS-PV, LukF-PV and integrase, complete cds
gi|2696710|dbj|AB006796.1|AB006796 [2696710]
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- ☐ U39769
Staphylococcus aureus 16S-23S ribosomal RNA spacer region
gi|2668542|gb|U39769.1|SAU39769 [2668542]
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- ☐ D00184
Staphylococcus aureus gene for staphylocoagulase, complete cds
gi|216976|dbj|D00184.1|STASCAG [216976]
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- ☐ X56628
Staphylococcus aureus qacA gene for antiseptic resistance protein
gi|773395|emb|X56628.1|SAQACA [773395]
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- ☐ AF033018
Staphylococcus aureus ribosome recycling factor (frr) gene, complete cds
gi|2645712|gb|AF033018.1|AF033018 [2645712]
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- ☐ AF034076
Staphylococcus aureus UDP-N-acetylmuramoyl-L-alanine synthetase (murC) gene, complete cds
gi|2642658|gb|AF034076.1|AF034076 [2642658]
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- ☐ D82063
Staphylococcus aureus gene for lipophilic protein, partial cds
gi|2641997|dbj|D82063.1|D82063 [2641997]
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- ☐ D76414
Staphylococcus aureus gene for histidyl-tRNA synthetase, ppGpp hydrolase, lytic enzyme, complete cds
gi|2580431|dbj|D76414.1|D76414 [2580431]
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- ☐ U57060
Staphylococcus aureus scdA gene, complete cds
gi|1575060|gb|U57060.1|SAU57060 [1575060]
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- ☐ D89066
Staphylococcus aureus DNA for DnaA, complete cds
gi|1854450|dbj|D89066.1|D89066 [1854450]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [2 MEDLINE links](#), or [1 protein link](#))
- ☐ U85095
Staphylococcus aureus strain KSI9051 agr signal transduction pathway genes: AgrB (agrB) gene, partial cds; pre-pheromone AgrD (agrD) and truncated sensor protein AgrC-31 (agrC) genes, complete cds; and transducer protein AgrA (agrA) gene, partial cds
gi|1916237|gb|U85095.1|SAU85095 [1916237]
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- ☐ U85097
Staphylococcus aureus strain RN4282 agr signal transduction pathway genes: AgrB (agrB) gene, partial cds, pre-pheromone AgrD (agrD) and sensor protein AgrC (agrC) genes, complete cds, and transducer protein AgrA (agrA) gene, partial cds
gi|1916245|gb|U85097.1|SAU85097 [1916245]
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- ☐ U85096
Staphylococcus aureus strain KSI54 agr signal transduction pathway genes: AgrB (agrB) gene, partial cds, pre-pheromone AgrD (agrD) and sensor protein AgrC (agrC) genes, complete cds,

and transducer protein AgrA (agrA) gene, partial cds

gi|1916241|gb|U85096.1|SAU85096 [1916241]

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☐ D42078

Staphylococcus aureus DNA for N-acetyl-glucosaminidase, partial cds

gi|2506026|dbj|D42078.1|D42078 [2506026]

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☐ AF015929

Staphylococcus aureus 16S ribosomal RNA gene, partial sequence

gi|2353761|gb|AF015929.1|AF015929 [2353761]

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☐ D10369

Staphylococcus aureus gene for glutamic acid-specific protease, partial cds

gi|2344764|dbj|D10369.1|D10369 [2344764]

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☐ A48955

Sequence 2 from Patent WO9604380

gi|2302593|emb|A48955.1|A48955 [2302593]

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☐ A48501

Sequence 3 from Patent WO9603516

gi|2302280|emb|A48501.1|A48501 [2302280]

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☐ A48500

Sequence 2 from Patent WO9603516

gi|2302278|emb|A48500.1|A48500 [2302278]

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☐ A48499

Sequence 1 from Patent WO9603516

gi|2302277|emb|A48499.1|A48499 [2302277]

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☐ A47600

Sequence 13 from Patent EP0688873

gi|2301548|emb|A47600.1|A47600 [2301548]

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- ☐ A47599
Sequence 12 from Patent EP0688873
gi|2301547|emb|A47599.1|A47599 [2301547]
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- ☐ A47598
Sequence 11 from Patent EP0688873
gi|2301546|emb|A47598.1|A47598 [2301546]
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- ☐ A47597
Sequence 10 from Patent EP0688873
gi|2301545|emb|A47597.1|A47597 [2301545]
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- ☐ A47596
Sequence 9 from Patent EP0688873
gi|2301544|emb|A47596.1|A47596 [2301544]
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- ☐ A47595
Sequence 8 from Patent EP0688873
gi|2301543|emb|A47595.1|A47595 [2301543]
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- ☐ A47594
Sequence 7 from Patent EP0688873
gi|2301542|emb|A47594.1|A47594 [2301542]
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- ☐ A44534
Sequence 10 from Patent WO9513395
gi|2299352|emb|A44534.1|A44534 [2299352]
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- ☐ A44533
Sequence 9 from Patent WO9513395
gi|2299351|emb|A44533.1|A44533 [2299351]
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- ☐ A44529
Sequence 5 from Patent WO9513395
gi|2299347|emb|A44529.1|A44529 [2299347]
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- ☐ A44528
Sequence 4 from Patent WO9513395
gi|2299346|emb|A44528.1|A44528 [2299346]

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☐ A44527

Sequence 3 from Patent WO9513395

gi|2299345|emb|A44527.1|A44527 [2299345]

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☐ A44526

Sequence 2 from Patent WO9513395

gi|2299344|emb|A44526.1|A44526 [2299344]

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☐ A44525

Sequence 1 from Patent WO9513395

gi|2299343|emb|A44525.1|A44525 [2299343]

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☐ A39696

Sequence 9 from Patent WO9418327

gi|2295954|emb|A39696.1|A39696 [2295954]

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☐ AF001783

Staphylococcus aureus strain RN8462 AgrB (agrB), AgrD (agrD) and AgrC (agrC) genes, complete cds

gi|2258297|gb|AF001783.1|AF001783 [2258297]

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☐ AF001782

Staphylococcus aureus strain SA502A AgrB (agrB), AgrD (agrD) and AgrC (agrC) genes, complete cds

gi|2258293|gb|AF001782.1|AF001782 [2258293]

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☐ L77194

Staphylococcus aureus peptidoglycan hydrolase (lytM) gene, complete cds

gi|2239273|gb|L77194.1|STALYTM [2239273]

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☐ AF003593

Staphylococcus aureus CspC (cspC) gene, complete cds

gi|2226348|gb|AF003593.1|AF003593 [2226348]

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- ☐ X74219
S.aureus gene for isoleucyl-tRNA synthetase
gi|437915|emb|X74219.1|SAILES [437915]
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- ☐ Y10419
S.aureus gene encoding outer surface binding 70kD protein, partial
gi|2190506|emb|Y10419.1|SAOSB70KD [2190506]
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- ☐ M63177
S.aureus sigma factor (plaC) gene, complete cds
gi|153068|gb|M63177.1|STAPLAC [153068]
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- ☐ E08773
DNA encoding Protein A
gi|2176885|dbj|E08773.1|E08773 [2176885]
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- ☐ E07163
Partial sequence of Staphylococcus aureus
gi|2175310|dbj|E07163.1|E07163 [2175310]
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- ☐ E07162
Partial sequence of Staphylococcus aureus
gi|2175309|dbj|E07162.1|E07162 [2175309]
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- ☐ E07161
Partial sequence of Staphylococcus aureus
gi|2175308|dbj|E07161.1|E07161 [2175308]
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- ☐ E07160
Partial sequence of *Staphylococcus aureus*
gi|2175307|dbj|E07160.1|E07160 [2175307]
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- ☐ E07159
Partial sequence of *Staphylococcus aureus*
gi|2175306|dbj|E07159.1|E07159 [2175306]
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- ☐ E07158
Partial sequence of *Staphylococcus aureus*
gi|2175305|dbj|E07158.1|E07158 [2175305]
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- ☐ E07157
Partial sequence of *Staphylococcus aureus*
gi|2175304|dbj|E07157.1|E07157 [2175304]
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- ☐ E07156
Partial sequence of *Staphylococcus aureus*
gi|2175303|dbj|E07156.1|E07156 [2175303]
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- ☐ E07155
Partial sequence of *Staphylococcus aureus*
gi|2175302|dbj|E07155.1|E07155 [2175302]
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- ☐ E03836
DNA encoding V8 protease
gi|2172050|dbj|E03836.1|E03836 [2172050]
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- ☐ E03835
DNA encoding V8-like protease
gi|2172049|dbj|E03835.1|E03835 [2172049]
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- ☐ E03526
gDNA encoding protein A
gi|2171742|dbj|E03526.1|E03526 [2171742]
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- ☐ E02873
DNA encoding staphylokinase(SAK)
gi|2171098|dbj|E02873.1|E02873 [2171098]
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- ☐ E01690
Genomic DNA of protein A of staphylococcus aureus
gi|2169943|dbj|E01690.1|E01690 [2169943]
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- ☐ E00876
DNA fragment comprising a promoter of sak gene and the region coding the signal peptide
gi|2169137|dbj|E00876.1|E00876 [2169137]
([View GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [10 nucleotide neighbors](#))
- ☐ E00203
DNA sequence of protein A-like molecule
gi|2168499|dbj|E00203.1|E00203 [2168499]
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- ☐ D83951
Staphylococcus aureus DNA for LukM component, LukF-PV like component, complete cds
gi|1230553|dbj|D83951.1|STALUK [1230553]
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- ☐ D17366
Staphylococcus aureus atl gene for autolysin, complete cds and other ORFs
gi|643603|dbj|D17366.1|STAATLA [643603]
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- ☐ D42144
Staphylococcus aureus gene for LUKM, complete cds
gi|577648|dbj|D42144.1|STAPLUKM [577648]
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- ☐ D42143
Staphylococcus aureus hlg2 gene for gamma-hemolysin, complete cds
gi|577646|dbj|D42143.1|STAHLG2 [577646]
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- ☐ D10489
Staphylococcus aureus genes for DNA gyrase A and B, complete cds
gi|540540|dbj|D10489.1|STAGYRABA [540540]

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☐ D21131

Staphylococcus aureus gene for a participant in homogeneous expression of high-level methicillin resistance, complete cds

gi|531264|dbj|D21131.1|STASRM551A [531264]

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☐ D30690

Staphylococcus aureus genes for ORF37; HSP20; HSP70; HSP40; ORF35, complete cds

gi|487326|dbj|D30690.1|STANHS [487326]

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☐ D14711

Staphylococcus aureus HSP10 and HSP60 genes

gi|441206|dbj|D14711.1|STAHSP [441206]

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☐ D90119

S. aureus norA gene

gi|216974|dbj|D90119.1|STANORA [216974]

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☐ D00730

S. aureus glutamic acid specific protease (EC 3.4.21.19) gene

gi|216970|dbj|D00730.1|STAGASP [216970]

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☐ D83357

Staphylococcus aureus (strain ATCC12600T) gene for 16S rRNA, partial sequence

gi|1199939|dbj|D83357.1|STA16SRR05 [1199939]

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☐ D83356

Staphylococcus aureus (strain OA1) gene for 16S rRNA, partial sequence

gi|1199938|dbj|D83356.1|STA16SRR04 [1199938]

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☐ D83355

Staphylococcus aureus (strain ATCC35844T) gene for 16S rRNA, partial sequence

gi|1199937|dbj|D83355.1|STA16SRR03 [1199937]

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- ☐ D83354
Staphylococcus aureus (strain Kitami) gene for 16S rRNA, partial sequence
gi|1199936|dbj|D83354.1|STA16SRR02 [1199936]
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- ☐ D83353
Staphylococcus aureus (strain FU16A2) gene for 16S rRNA, partial sequence
gi|1199935|dbj|D83353.1|STA16SRR01 [1199935]
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- ☐ D12572
Staphylococcus aureus rrnA gene for 23S ribosomal RNA
gi|216969|dbj|D12572.1|STA23SRNA [216969]
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- ☐ D86727
Staphylococcus aureus DNA for DNA polymerase III, complete cds
gi|1483181|dbj|D86727.1|D86727 [1483181]
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- ☐ D86240
Staphylococcus aureus gene for unkown function and dlt operon dltA, dltB, dltC and dltD genes, complete cds
gi|1405333|dbj|D86240.1|D86240 [1405333]
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- ☐ D67075
Staphylococcus aureus DNA for DNA topoisomerase IV GrIB subunit, DNA topoisomerase IV GrIA subunit, complete cds
gi|1777319|dbj|D67075.1|D67075 [1777319]
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- ☐ D67074
Staphylococcus aureus DNA for DNA topoisomerase IV GrIB subunit, DNA topoisomerase IV GrIA subunit, complete cds
gi|1777316|dbj|D67074.1|D67074 [1777316]
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- ☐ U97062
Staphylococcus aureus NCTC 8325 SecA (secA) gene, complete cds
gi|2078389|gb|U97062.1|SAU97062 [2078389]
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- ☐ U96620
Staphylococcus aureus NCTC 8325 ribosomal protein L30 (L30), ribosomal protein L15 (L15) and SecY (secY) genes, complete cds
gi|2078379|gb|U96620.1|SAU96620 [2078379]
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- ☐ U96619
Staphylococcus aureus NCTC 8325 SecE (secE), NusG (nusG) and RplK (rplK) genes, complete cds
gi|2078375|gb|U96619.1|SAU96619 [2078375]
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- ☐ Z84573
S.aureus dihydropteroate synthase gene
gi|2058355|emb|Z84573.1|SADHPS01 [2058355]
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- ☐ AB001896
Staphylococcus aureus DNA for sigma70 operon, complete cds
gi|1943991|dbj|AB001896.1|AB001896 [1943991]
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- ☐ Y07645
S.aureus sigB gene
gi|1934986|emb|Y07645.1|SASIGFACB [1934986]
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- ☐ U92441
Staphylococcus aureus alkyl hydroperoxide reductase subunit C (aphC) and subunit F (aphF) genes, complete cds
gi|1916315|gb|U92441.1|SAU92441 [1916315]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [1 MEDLINE link](#), or [2 protein links](#))
- ☐ U91741
Staphylococcus aureus teichoic acid biosynthesis TagB gene, partial cds and TagX and TagD genes, complete cds
gi|1913904|gb|U91741.1|SAU91741 [1913904]
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- ☐ U29454
Staphylococcus aureus penicillin binding protein 4 (pbpD) gene, complete cds
gi|1905928|gb|U29454.1|SAU29454 [1905928]
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□ U29478

Staphylococcus aureus ABC transporter-like protein AbcA (abcA) gene, complete cds
gi|1841513|gb|U29478.1|SAU29478 [1841513]
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- ☐ U73374
Staphylococcus aureus type 8 capsule genes, cap8A, cap8B, cap8C, cap8D, cap8E, cap8F, cap8G, cap8H, cap8I, cap8J, cap8K, cap8L, cap8M, cap8N, cap8O, cap8P, complete cds
gi|1657639|gb|U73374.1|SAU73374 [1657639]
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- ☐ L42945
Staphylococcus aureus lytS and lytR genes, complete cds
gi|1854576|gb|L42945.1|STALYTS [1854576]
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- ☐ U38429
Staphylococcus aureus chloramphenicol resistance plasmid pKH7, complete sequence
gi|1731451|gb|U38429.1|SAU38429 [1731451]
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- ☐ U81980
Staphylococcus aureus plasmid pKH4 replication protein Rep (rep) and quaternary ammonium compounds resistance protein Qac genes, complete cds
gi|1848267|gb|U81980.1|SAU81980 [1848267]
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- ☐ X55185
S. aureus hla gene for truncated alpha-toxin
gi|46745|emb|X55185.1|SATAT [46745]
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- ☐ V01278
S.aureus plasmid pE194 ORF's A,B,C,D,E, and F
gi|46555|emb|V01278.1|SAE194 [46555]
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- ☐ U31979
Staphylococcus aureus chorismate synthase (aroC) and nucleoside diphosphate kinase (ndk) genes, complete cds, dehydroauinate synthase (aroB) and geranylgeranyl pyrophosphate synthetase homolog (gerCC) genes, partial cds
gi|987495|gb|U31979.1|SAU31979 [987495]
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- ☐ X91786
S.aureus abcA, pbp4, and tagD genes
gi|1262135|emb|X91786.1|SAPBP4GEN [1262135]
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- ☐ U36912
Staphylococcus aureus plasmid J3356::POX7;3, complete sequence
gi|1045528|gb|U36912.1|SAU36912 [1045528]
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- ☐ U36911
Staphylococcus aureus plasmid J3356::POX7;1, complete sequence
gi|1045526|gb|U36911.1|SAU36911 [1045526]
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- ☐ U36910
Staphylococcus aureus plasmid J3358, complete sequence
gi|1045523|gb|U36910.1|SAU36910 [1045523]
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- ☐ U64885
Staphylococcus aureus ribonuclease P RNA (rnpB) gene, partial sequence
gi|1498078|gb|U64885.1|SAU64885 [1498078]
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- ☐ U76872
Staphylococcus aureus isolate EMRSA-9 coagulase gene, VNTR sequence, sequence tagged site
gi|1753154|gb|U76872.1|SAU76872 [1753154]
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- ☐ U76871
Staphylococcus aureus isolate EMRSA-9 coagulase gene, VNTR sequence, sequence tagged site
gi|1753153|gb|U76871.1|SAU76871 [1753153]
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- ☐ U76870
Staphylococcus aureus isolate EMRSA-2 coagulase gene, VNTR sequence, sequence tagged site
gi|1753152|gb|U76870.1|SAU76870 [1753152]
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- ☐ U76869
Staphylococcus aureus isolate EMRSA-2 coagulase gene, VNTR sequence, sequence tagged site
gi|1753151|gb|U76869.1|SAU76869 [1753151]
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- ☐ U76868
Staphylococcus aureus isolate EMRSA-16 coagulase gene, VNTR sequence, sequence tagged site
gi|1753150|gb|U76868.1|SAU76868 [1753150]
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- ☐ U76867
Staphylococcus aureus isolate EMRSA-16 coagulase gene, VNTR sequence, sequence tagged site
gi|1753149|gb|U76867.1|SAU76867 [1753149]
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- ☐ U76866
Staphylococcus aureus isolate EMRSA-15 coagulase gene, VNTR sequence, sequence tagged site
gi|1753148|gb|U76866.1|SAU76866 [1753148]
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- ☐ U76865
Staphylococcus aureus isolate EMRSA-5 coagulase gene, VNTR sequence, sequence tagged site
gi|1753147|gb|U76865.1|SAU76865 [1753147]
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- ☐ U76864
Staphylococcus aureus isolate EMRSA-12 coagulase gene, VNTR sequence, sequence tagged site
gi|1753146|gb|U76864.1|SAU76864 [1753146]
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- ☐ U76863
Staphylococcus aureus isolate EMRSA-6 coagulase gene, VNTR sequence, sequence tagged site
gi|1753145|gb|U76863.1|SAU76863 [1753145]
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- ☐ U76862
Staphylococcus aureus isolate EMRSA-10 coagulase gene, VNTR sequence, sequence tagged site
gi|1753144|gb|U76862.1|SAU76862 [1753144]
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- ☐ U76861
Staphylococcus aureus isolate Jevons coagulase gene, VNTR sequence, sequence tagged site
gi|1753143|gb|U76861.1|SAU76861 [1753143]
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- ☐ U76860
Staphylococcus aureus isolate EMRSA-3 coagulase gene, VNTR sequence, sequence tagged site
gi|1753142|gb|U76860.1|SAU76860 [1753142]
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- ☐ U76859
Staphylococcus aureus isolate EMRSA-14 coagulase gene, VNTR sequence, sequence tagged site
gi|1753141|gb|U76859.1|SAU76859 [1753141]
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- ☐ U76858
Staphylococcus aureus German coagulase gene, VNTR sequence, sequence tagged site
gi|1753140|gb|U76858.1|SAU76858 [1753140]
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- ☐ U76857
Staphylococcus aureus isolate ps42e coagulase gene, VNTR sequence, sequence tagged site
gi|1753139|gb|U76857.1|SAU76857 [1753139]
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- ☐ U76856
Staphylococcus aureus isolate EMRSA-7 coagulase gene, VNTR sequence, sequence tagged site
gi|1753138|gb|U76856.1|SAU76856 [1753138]
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- ☐ U76855
Staphylococcus aureus isolate EMRSA-1 coagulase gene, VNTR sequence, sequence tagged site
gi|1753137|gb|U76855.1|SAU76855 [1753137]
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- ☐ U76854
Staphylococcus aureus isolate EMRSA-4 coagulase gene, VNTR sequence, sequence tagged site
gi|1753136|gb|U76854.1|SAU76854 [1753136]
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- ☐ U76853
Staphylococcus aureus isolate EMRSA-1 coagulase gene, VNTR sequence, sequence tagged site
gi|1753135|gb|U76853.1|SAU76853 [1753135]
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- ☐ U76852
Staphylococcus aureus isolate EMRSA-11 coagulase gene, VNTR sequence, sequence tagged site
gi|1753134|gb|U76852.1|SAU76852 [1753134]
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- ☐ U76851
Staphylococcus aureus isolate EMRSA-15 coagulase gene, VNTR sequence, sequence tagged site
gi|1753133|gb|U76851.1|SAU76851 [1753133]
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- ☐ U76850
Staphylococcus aureus isolate ps 71 coagulase gene, VNTR sequence, sequence tagged site
gi|1753132|gb|U76850.1|SAU76850 [1753132]
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- ☐ U76849
Staphylococcus aureus isolate EMRSA-13 coagulase gene, VNTR sequence, sequence tagged site
gi|1753131|gb|U76849.1|SAU76849 [1753131]
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- ☐ U76848
Staphylococcus aureus isolate EMRSA-15 coagulase gene, VNTR sequence, sequence tagged

site

gi|1753130|gb|U76848.1|SAU76848 [1753130]

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☐ U76847

Staphylococcus aureus isolate EMRSA-15 coagulase gene, VNTR sequence, sequence tagged site

gi|1753129|gb|U76847.1|SAU76847 [1753129]

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☐ Y09929

S.aureus rsbU, rsbV, rsbW & sigB genes

gi|1729791|emb|Y09929.1|SAUSIGB [1729791]

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☐ Y09570

S.aureus femD gene

gi|1684748|emb|Y09570.1|SAFEMD [1684748]

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☐ X95848

S.aureus fnbA gene

gi|1204145|emb|X95848.1|SAFNBA [1204145]

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☐ Y09428

S.aureus rpoC gene

gi|1684750|emb|Y09428.1|SARPOCGE1 [1684750]

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☐ S76611

{dru element, hypervariable region, methicillin resistance determinant} [Staphylococcus aureus, MRSA, HVR genotype B, Genomic, 411 nt]

gi|913625|gb|S76611.1|S76611 [913625]

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☐ S76213

asp23=alkaline shock protein 23 {methicillin resistant} [Staphylococcus aureus, 912, Genomic, 1360 nt]

gi|894288|gb|S76213.1|S76213 [894288]

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☐ S75707

mec A {5' region, mutation IV} [Staphylococcus aureus, methicillin-resistant MR108, Genomic Mutant, 67 nt]
gi|913672|gb|S75707.1|S75707 [913672]
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☐ S75706
mec A {5' region, mutation III} [Staphylococcus aureus, methicillin-resistant MR108, Genomic Mutant, 67 nt]
gi|913671|gb|S75706.1|S75706 [913671]
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☐ S75705
mec A {5' region, mutation II} [Staphylococcus aureus, methicillin-resistant MR108, Genomic Mutant, 67 nt]
gi|913670|gb|S75705.1|S75705 [913670]
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☐ S76270
16S rRNA {16S-23S ribosomal RNA intergenic region} [Staphylococcus aureus, clinical isolate, Genomic, 94 nt]
gi|894286|gb|S76270.1|S76270 [894286]
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☐ S72497
plc=beta-hemolysin [Staphylococcus aureus, 126/89, Genomic, 1308 nt]
gi|619316|gb|S72497.1|S72497 [619316]
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☐ S72488
hemB=prophobilinogen synthase [Staphylococcus aureus, SA1959, Genomic, 1087 nt]
gi|632815|gb|S72488.1|S72488 [632815]
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- ☐ S74031
norA=NorA {ISP794} [Staphylococcus aureus, NCTC 8325, Insertion, 1820 nt]
gi|693734|gb|S74031.1|S74031 [693734]
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- ☐ S67449
tet(K)=tetracycline efflux protein [Staphylococcus aureus, pT181, Plasmid, 1380 nt]
gi|456769|gb|S67449.1|S67449 [456769]
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- ☐ U75367
Staphylococcus aureus transposon Tn551 transposase gene, partial cds
gi|1673526|gb|U75367.1|SATN551S2 [1673526]
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- ☐ U75368
Staphylococcus aureus transposon Tn551 transposase gene, partial cds
gi|1673524|gb|U75368.1|SATN551S1 [1673524]
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- ☐ U31175
Staphylococcus aureus D-specific D-2-hydroxyacid dehydrogenase (ddh) gene, complete cds
gi|1644432|gb|U31175.1|SAU31175 [1644432]
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- ☐ X53096
S.aureus genes encoding Sau96I DNA methyltransferase and Sau96I restriction endonuclease
gi|46616|emb|X53096.1|SAMTRE [46616]
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- ☐ X53951
S.aureus plasmid pSH6 DNA for insertion sequences IS257-2, IS257-3 and IS256

gi|46598|emb|X53951.1|SAIS2572 [46598]

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☐ X53952

S.aureus plasmid pSH6 DNA for insertion sequences IS257-1 and IS256

gi|46596|emb|X53952.1|SAIS2571 [46596]

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☐ X03408

Staphylococcus aureus plasmid pUB110dB sequence

gi|46495|emb|X03408.1|SA110KAR [46495]

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☐ U50629

Staphylococcus aureus nicking enzyme (nes) gene, complete cds

gi|1245473|gb|U50629.1|SAU50629 [1245473]

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☐ U38656

Staphylococcus aureus tetracycline resistance plasmid pKH1, tet gene, complete cds

gi|1580803|gb|U38656.1|SAU38656 [1580803]

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☐ U58139

Staphylococcus aureus beta-lactamase (blaz) gene, complete cds

gi|1575124|gb|U58139.1|SAU58139 [1575124]

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☐ A31894

S.aureus pUB110 Ble gene

gi|1567207|emb|A31894.1|A31894 [1567207]

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☐ L42943

Staphylococcus aureus (clone KIN50) phosphoenolpyruvate carboxykinase (pckA) gene, complete cds

gi|860731|gb|L42943.1|STAPEPCK [860731]

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☐ U51474

Staphylococcus aureus truncated streptothricin acetyl transferase (sat) and 3'5'-aminoglycoside phosphotransferase (aphA-3) genes, complete cds

gi|1272325|gb|U51474.1|SAU51474 [1272325]

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☐ U50077

Staphylococcus aureus multidrug resistance plasmid pKH8 replication protein (rep) gene, qacC' gene, and multidrug resistance protein (qacC) gene, complete cds

gi|1236637|gb|U50077.1|SAU50077 [1236637]

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☐ U38428

Staphylococcus aureus tetracycline resistance plasmid pKH6, complete sequence

gi|1052997|gb|U38428.1|SAU38428 [1052997]

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☐ U66665

Staphylococcus aureus DNA fragment with class II promoter activity

gi|1519432|gb|U66665.1|SAU66665 [1519432]

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☐ U66664

Staphylococcus aureus DNA fragment with class II promoter activity

gi|1519431|gb|U66664.1|SAU66664 [1519431]

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☐ U66663

Staphylococcus aureus DNA fragment with class II promoter activity

gi|1519430|gb|U66663.1|SAU66663 [1519430]

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☐ X87104

S.aureus mdr, pbp4 and taqD genes (SG511-55 isolate)

gi|1125684|emb|X87104.1|SADNAS55 [1125684]

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☐ X87105

S.aureus mdr, pbp4 and taqD genes (PVI-25 isolate)

gi|1125680|emb|X87105.1|SADNAS25 [1125680]

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☐ X89233

S.aureus DNA for rpoC gene

gi|1495790|emb|X89233.1|SARPOCGEN [1495790]

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- ☐ M28521
Staphylococcus aureus enterotoxin D (entD) gene, complete cds
gi|1492109|gb|M28521.1|STAENTD [1492109]
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- ☐ U54636
Staphylococcus aureus protein A, complete cds
gi|1480566|gb|U54636.1|SAU54636 [1480566]
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- ☐ U46541
Staphylococcus aureus sarA gene, complete cds
gi|1477531|gb|U46541.1|SAU46541 [1477531]
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- ☐ L14017
Staphylococcus aureus methicillin-resistance protein (mecR) gene and unknown ORF, complete cds
gi|1408062|gb|L14017.1|STAMECRA [1408062]
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- ☐ U60589
Staphylococcus aureus novel antigen gene, complete cds
gi|1407783|gb|U60589.1|SAU60589 [1407783]
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- ☐ Z48003
S.aureus gene for DNA polymerase III
gi|642269|emb|Z48003.1|SADNAPOL3 [642269]
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- ☐ M37889
Staphylococcus aureus replication (rep), control of replication (cop), and resistance protein (QacC) genes, complete cds
gi|153091|gb|M37889.1|STAREPQAC [153091]
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- ☐ V01281
S.aureus mRNA for nuclease
gi|46623|emb|V01281.1|SANUCX [46623]
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- ☐ X97985
S.aureus orfs 1,2,3 & 4
gi|1340127|emb|X97985.1|SA1234 [1340127]
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- ☐ X00127
Staphylococcus aureus S-phi-C gene for staphylokinase
gi|47425|emb|X00127.1|SPSAK1 [47425]
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- ☐ X03286
Staphylococcus aureus mutant strain V1 spa gene for protein A
gi|46774|emb|X03286.1|SAV1SPA [46774]
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- ☐ X62282
S.aureus target site DNA for IS431 insertion
gi|46769|emb|X62282.1|SATSIS431 [46769]
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- ☐ X01645
Staphylococcus aureus (Wood 46) gene for alpha-toxin
gi|46763|emb|X01645.1|SATOXA [46763]
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- ☐ X16471
Staphylococcus aureus transposon Tn4002 blaZ gene for beta-lactamase
gi|46761|emb|X16471.1|SATNBLAZ [46761]
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- ☐ X52734
S.aureus Tn552 transposable element
gi|46754|emb|X52734.1|SATN552 [46754]
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- ☐ X13290
Staphylococcus aureus multi-resistance plasmid pSK1 DNA containing transposon Tn4003
gi|46747|emb|X13290.1|SATN4003 [46747]
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- ☐ X66088
S.aureus tRNA-Asp gene

gi|46744|emb|X66088.1|SATASP [46744]

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☐ Z30588

S.aureus (RN4220) genes for potential ABC transporter and potential membrane spanning protein

gi|459255|emb|Z30588.1|SASTPSMP [459255]

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☐ X16457

Staphylococcus aureus gene for staphylocoagulase

gi|46736|emb|X16457.1|SASTPHLC [46736]

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☐ X00342

Staphylococcus aureus 3' end of the gene for protein A

gi|46694|emb|X00342.1|SASPAY [46694]

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☐ V01287

Staphylococcus aureus gene (spa) fragment encoding protein A

gi|46692|emb|V01287.1|SASPAX [46692]

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☐ X61307

Staphylococcus aureus spa gene for protein A

gi|46690|emb|X61307.1|SASPAPA [46690]

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☐ Y00356

Staphylococcus aureus V8 serine protease gene

gi|46686|emb|Y00356.1|SASP [46686]

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☐ X06603

Staphylococcus aureus phage 42D for staphylokinase

gi|46676|emb|X06603.1|SASAK42D [46676]

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☐ X93205

S.aureus ptsH and ptsI genes

gi|1070384|emb|X93205.1|SAPTSHI [1070384]

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nucleotide neighbors)

☐ X64172

S.aureus rplL, orf202, rpoB(rif) and rpoC genes for ribosomal protein L7/L12, hypothetical protein ORF202, DNA-directed RNA polymerase beta & beta' chains
gi|677848|emb|X64172.1|SARPLRPO [677848]
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☐ X72700

S.aureus genes for S and F components of Pantone-Valentine leucocidins
gi|551668|emb|X72700.1|SAPVLSF [551668]
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- ☐ X60827
S.aureus (plasmid pSCS6) cat gene for chloramphenicol acetyltransferase
gi|46651|emb|X60827.1|SAPSCS6 [46651]
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- ☐ X64389
S.aureus leuF-P83 gene for F component of leucocidin R
gi|488528|emb|X64389.1|SALEUF [488528]
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- ☐ X62288
S.aureus DNA for penicillin-binding protein 2
gi|483533|emb|X62288.1|SAPENBP2 [483533]
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- ☐ X55798
S.aureus plasmid pOX2000
gi|295833|emb|X55798.1|SAPOX2000 [295833]
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- ☐ X58434
S.aureus pdhB, pdhC and pdhD genes for pyruvate decarboxylase, dihydrolipoamide acetyltransferase and dihydrolipoamide dehydrogenase
gi|48871|emb|X58434.1|SAPDHDNA [48871]
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- ☐ X06627
Staphylococcus aureus plasmid pS194 sequence
gi|46643|emb|X06627.1|SAPS194 [46643]
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- ☐ X12831
Staphylococcus aureus chloramphenicol resistance plasmid pC223 DNA (nt 1250 - 3072)

gi|46637|emb|X12831.1|SAPC223A [46637]
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☐ X07371

Staphylococcus aureus plasmid pC223 basic replicon DNA
gi|46635|emb|X07371.1|SAPC223 [46635]
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☐ X02529

Staphylococcus aureus plasmid pC221 complete DNA sequence
gi|46630|emb|X02529.1|SAPC221 [46630]
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☐ Y00688

Staphylococcus aureus (MRSA) PBP gene for beta-lactam-inducible penicillin-binding protein
gi|46628|emb|Y00688.1|SAPBP [46628]
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☐ X04121

S. aureus PC1 beta-lactamase gene blaZ from plasmid pI258
gi|46626|emb|X04121.1|SAPBLAZ [46626]
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☐ X59477

S.aureus plasmid DNA for part of mupirocin resistance gene (XhoI site)
gi|46621|emb|X59477.1|SAMUPIRES [46621]
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☐ X59478

S.aureus plasmid DNA for mupirocin resistance gene (NcoI-NcoI fragment)
gi|46619|emb|X59478.1|SAMUPIREI [46619]
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☐ X63598

S.aureus mecR1 and mecI genes
gi|46612|emb|X63598.1|SAMECR1I [46612]
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☐ X52593

S. aureus mecA gene for PBP2' (penicillin binding protein 2')
gi|46610|emb|X52593.1|SAMECAPB [46610]
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- ☐ X76490
S.aureus (bb270) glnA and glnR genes
gi|1134885|emb|X76490.1|SAGLNAR [1134885]
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- ☐ X81586
S.aureus hlgA, hlgB and hlgC genes
gi|550421|emb|X81586.1|SAHLGABC [550421]
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- ☐ X72014
S.aureus fib gene for fibrinogen-binding protein
gi|311975|emb|X72014.1|SAFIBB [311975]
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- ☐ X72013
S.aureus fib gene for fibrinogen-binding protein
gi|311973|emb|X72013.1|SAFIBA [311973]
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- ☐ X71437
S.aureus genes gyrB, gyrA and recF (partial)
gi|296393|emb|X71437.1|SAGYRREC [296393]
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- ☐ X62992
S.aureus fnbB gene for fibronectin binding protein B
gi|49040|emb|X62992.1|SAFNBB [49040]
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- ☐ X52594
S. aureus hypervariable region, 3' to mecA gene
gi|48712|emb|X52594.1|SAHVR [48712]
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- ☐ X14827
Staphylococcus aureus lacC and lacD genes
gi|46604|emb|X14827.1|SALACCD [46604]
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- ☐ X13404

Staphylococcus aureus hlb gene for beta-hemolysin

gi|46586|emb|X13404.1|SAHLB [46586]

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☐ X17301

S.aureus DNA for hld gene and for part of agr gene

gi|46585|emb|X17301.1|SAHDLAGR [46585]

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☐ X17688

S.aureus factor essential for expression of methicillin resistance (femA) gene, complete cds, and trpA gene, 3' end

gi|46579|emb|X17688.1|SAFEMA [46579]

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☐ X03097

Staphylococcus aureus plasmid pE194 mRNA for ermC leader region

gi|46574|emb|X03097.1|SAERMCTR [46574]

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☐ Z16422

S.aureus dfrB gene for dihydrofolate reductase

gi|671631|emb|Z16422.1|SADIRED [671631]

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☐ Z33409

S.aureus (C6-coa-EM) coagulase gene repeat region

gi|495298|emb|Z33409.1|SACOAGR6 [495298]

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☐ Z33408

S.aureus (C50-coa-E) coagulase gene repeat region

gi|495297|emb|Z33408.1|SACOAGR5 [495297]

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☐ Z33407

S.aureus (C35-coa-E) coagulase gene repeat region

gi|495296|emb|Z33407.1|SACOAGR4 [495296]

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☐ Z33406

S.aureus (C26-coa-E) coagulase gene repeat region

gi|495295|emb|Z33406.1|SACOAGR3 [495295]

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☐ Z33405

S.aureus (C20-coa-E) coagulase gene repeat region
gi|495294|emb|Z33405.1|SACOAGR2 [495294]

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☐ Z33404

S.aureus (C14-coa-E) coagulase gene repeat region
gi|495293|emb|Z33404.1|SACOAGR1 [495293]

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☐ X75439

S.aureus plasmid encoded DNA, mup R gene
gi|438226|emb|X75439.1|SADNAMUPR [438226]

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☐ X62587

S.aureus ebr gene for ethidium bromide resistance protein
gi|49016|emb|X62587.1|SAEBRN20 [49016]

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☐ X54338

S.aureus plasmid pA22 ermC gene (5' region)
gi|46572|emb|X54338.1|SAERMC [46572]

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☐ X51661

S.aureus enterotoxin C3 gene (entC3)
gi|46570|emb|X51661.1|SAENTC3A [46570]

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☐ X05815

Staphylococcus enterotoxin C1 gene (entC1)
gi|46566|emb|X05815.1|SAENTC1 [46566]

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☐ X15574

Staphylococcus aureus plasmid gene for ethidium bromide resistance (ebr)
gi|46560|emb|X15574.1|SAEBR [46560]

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- ☐ Y07536
S. aureus genes for thymidylate synthetase and dihydrofolate reductase type S1 in plasmid pABU1
gi|46551|emb|Y07536.1|SADHFR [46551]
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- ☐ X02166
Staphylococcus plasmid pC221
gi|46545|emb|X02166.1|SACP221 [46545]
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- ☐ Z49245
S.aureus partial sod gene for superoxide dismutase
gi|806584|emb|Z49245.1|SA4220SOD [806584]
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- ☐ X16298
Staphylococcus aureus plasmid pI9789 DNA with binR and bin3 genes, derived from transposon TN552
gi|398181|emb|X16298.1|SABINR3 [398181]
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- ☐ Z18852
S.aureus gene for clumping factor
gi|397525|emb|Z18852.1|SACFG [397525]
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- ☐ X68417
S.aureus gene for 16S rRNA
gi|312111|emb|X68417.1|SA16SRRN [312111]
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- ☐ X68425
S.aureus gene for 23S rRNA
gi|288516|emb|X68425.1|SA23SRRN [288516]
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- ☐ X17679
Staphylococcus aureus coa gene for coagulase
gi|46539|emb|X17679.1|SACOA [46539]
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X63072

S.aureus DNA for cat transcription terminator region

ugi|46538|emb|X63072.1|SACATTERM [46538]

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 X02872

Staphylococcus aureus plasmid pUB112 CAT-gene for chloramphenicol acetyltransferase

gi|46536|emb|X02872.1|SACATG [46536]

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- ☐ V01277
Staphylococcus aureus plasmid pC194. Includes gene for chloramphenicol acetyl transferase and three further genes (one of which is necessary for replication)
gi|46531|emb|V01277.1|SAC194 [46531]
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- ☐ X52543
S.aureus agrA, agrB and hld genes
gi|46505|emb|X52543.1|SAAGRAB [46505]
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- ☐ A19943
SEQ ID NO: 8, strain 1335 nucleotide probe
gi|580681|emb|A19943.1|A19943 [580681]
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- ☐ A19942
SEQ ID NO: 7, strain 06231 nucleotide probe
gi|580680|emb|A19942.1|A19942 [580680]
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- ☐ A19941
SEQ ID NO: 6, strain 215C nucleotide probe
gi|580679|emb|A19941.1|A19941 [580679]
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- ☐ A19940
SEQ ID NO: 5, strain 214 nucleotide probe
gi|580678|emb|A19940.1|A19940 [580678]
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- ☐ A19939

SEQ ID NO: 4, strain 02599 nucleotide probe
gi|580677|emb|A19939.1|A19939 [580677]
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☐ A19938
SEQ ID NO: 3, strain A216 nucleotide probe
gi|580676|emb|A19938.1|A19938 [580676]
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☐ A19937
SEQ ID NO: 2, strain 00646 nucleotide probe
gi|580675|emb|A19937.1|A19937 [580675]
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☐ A19936
SEQ ID NO: 1, strain 05723 nucleotide probe
gi|580674|emb|A19936.1|A19936 [580674]
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☐ A17958
sau3AI R and sau3AI M coding region
gi|512529|emb|A17958.1|A17958 [512529]
([View GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [2 protein links](#))

☐ A12915
S.aureus DNA (pSDF203) for fibronectin binding protein (partial)
gi|512507|emb|A12915.1|A12915 [512507]
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☐ A12913
S.aureus DNA (pSDF102) for fibronectin binding protein (partial)
gi|512506|emb|A12913.1|A12913 [512506]
([View GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [8 nucleotide neighbors](#))

☐ A12906
S.aureus DNA for fibronectin binding protein (partial)
gi|512505|emb|A12906.1|A12906 [512505]
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☐ A12905
S.aureus DNA for fibronectin binding protein (partial)
gi|512503|emb|A12905.1|A12905 [512503]
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- ☐ A12904
S.aureus DNA for fibronectin binding protein (partial)
gi|512501|emb|A12904.1|A12904 [512501]
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- ☐ A12903
S.aureus DNA for fibronectin binding protein (partial)
gi|512499|emb|A12903.1|A12903 [512499]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [1 protein link](#), or [6 nucleotide neighbors](#))
- ☐ A12902
S.aureus DNA for fibronectin binding protein (partial)
gi|512497|emb|A12902.1|A12902 [512497]
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- ☐ A12901
S.aureus DNA for fibronectin binding protein (partial)
gi|512495|emb|A12901.1|A12901 [512495]
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- ☐ A12900
S.aureus DNA for fibronectin binding protein (partial)
gi|512494|emb|A12900.1|A12900 [512494]
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- ☐ A12899
S.aureus DNA for fibronectin binding protein (partial)
gi|512492|emb|A12899.1|A12899 [512492]
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- ☐ A12898
S.aureus DNA for fibronectin binding protein (partial)
gi|512490|emb|A12898.1|A12898 [512490]
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- ☐ A12897
S.aureus DNA for fibronectin binding protein (partial)
gi|512488|emb|A12897.1|A12897 [512488]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), [1 protein link](#), or [3 nucleotide neighbors](#))
- ☐ A12896

S.aureus DNA for fibronectin binding protein (partial)

gi|512486|emb|A12896.1|A12896 [512486]

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☐ A09523

S.aureus Arp 4 gene

gi|412258|emb|A09523.1|A09523 [412258]

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☐ A04518

S.aureus gene for structural protein A, duplicate

gi|412213|emb|A04518.1|A04518 [412213]

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☐ A04517

S.aureus gene for structural protein A

gi|412212|emb|A04517.1|A04517 [412212]

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☐ A04512

S.aureus gene for structural protein A

gi|412210|emb|A04512.1|A04512 [412210]

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☐ L41499

Staphylococcus aureus ORF1, partial cds, ORF2, ORF3, autolysin (atl) genes, complete cds

gi|765069|gb|L41499.1|STAATL [765069]

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☐ U19770

Staphylococcus aureus pyrrolidone carboxyl peptidase (pcp) gene, complete cds

gi|790572|gb|U19770.1|SAU19770 [790572]

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☐ X53818

S. aureus IS431mec gene associated with methicillin resistance

gi|46601|emb|X53818.1|SAIS431M [46601]

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☐ M20129

Staphylococcus aureus vgh gene, complete cds

gi|153076|gb|M20129.1|STAPVGHG [153076]

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protein link, or 19 nucleotide neighbors)

☐ L43098

Transposon Tn5404 and insertion sequences IS1181 and IS1182 (from *Staphylococcus aureus*) DNA

gi|1280355|gb|L43098.1|INSTN5405R [1280355]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, or 6 nucleotide neighbors)

☐ L43082

Transposon Tn5405 and insertion sequence IS1182 (from *Staphylococcus aureus*) ORFA and transposase gene, complete cds

gi|1280353|gb|L43082.1|INSTN5405L [1280353]

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☐ X03216

Staphylococcus aureus transposon Tn554

gi|43726|emb|X03216.1|ISTN554 [43726]

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☐ X70648

S. aureus 16S rRNA (partial)

gi|46498|emb|X70648.1|SA16S [46498]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 MEDLINE link, or 1075 nucleotide neighbors)

☐ U51133

Staphylococcus aureus phosphoenolpyruvate carboxykinase (pckA) gene, complete cds

gi|1255261|gb|U51133.1|SAU51133 [1255261]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 protein link, or 4 nucleotide neighbors)

☐ U51132

Staphylococcus aureus o-succinylbenzoic acid CoA ligase (mene), and o-succinylbenzoic acid synthetase (menc) genes, complete cds

gi|1255258|gb|U51132.1|SAU51132 [1255258]

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☐ X02588

S. aureus Tn554 spc gene for sp adenylyltransferase AAD(9) (sp = spectinomycin)

gi|46696|emb|X02588.1|SASPCG [46696]

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☐ X61716

S. aureus hlb gene encoding sphingomyelinase

gi|46590|emb|X61716.1|SAHLBG [46590]

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- ☐ X61719
S.aureus phi-13 lysogen right chromosome/bacteriophage DNA junction
gi|46625|emb|X61719.1|SAP13RJNC [46625]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [1 MEDLINE link](#))
- ☐ X61718
S.aureus phi-13 lysogen left chromosomal/bacteriophage DNA junction
gi|46624|emb|X61718.1|SAP13LJNC [46624]
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- ☐ X67743
S.aureus (strain 42CR3-L) right junction DNA
gi|46518|emb|X67743.1|SAATTB2 [46518]
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- ☐ X67742
S.aureus (strain 42CR3-L) left junction DNA
gi|46517|emb|X67742.1|SAATTB1 [46517]
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- ☐ X67741
S.aureus (strain A3CR3-L) left junction DNA
gi|46516|emb|X67741.1|SAATTSA2 [46516]
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- ☐ X67740
S.aureus (strain A3CR3-L) right junction DNA
gi|46515|emb|X67740.1|SAATTSA1 [46515]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [1 MEDLINE link](#))
- ☐ X67738
S.aureus (strain 80CR3) attB gene
gi|46514|emb|X67738.1|SAATTBA [46514]
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- ☐ U02910
Staphylococcus aureus ATCC 25923 16S rRNA gene, partial sequence
gi|455053|gb|U02910.1|SAU02910 [455053]
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- ☐ AH003349
Transposon IS431 (from S.aureus penicillinase plasmid pI524), 5' copy
gi|154887|gb|AH003349.1|SEG_TRN431 [154887]
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☐ M11118

S.aureus enterotoxin B gene, complete cds

gi|152999|gb|M11118.1|STAENTB [152999]

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- ☐ M18086
S.aureus transposon 4001 aacA-aphD aminoglycoside resistance gene, complete cds, and right and left IS256 transposase genes
gi|152946|gb|M18086.1|STAAGLSRA [152946]
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- ☐ U19459
Staphylococcus aureus acetyltransferase VAT B (vat B) gene, complete cds
gi|1181626|gb|U19459.1|SAU19459 [1181626]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [1 protein link](#))
- ☐ U35773
Staphylococcus aureus prolipoprotein diacylglycerol transferase (lgt) gene, complete cds
gi|1016769|gb|U35773.1|SAU35773 [1016769]
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- ☐ U26702
Staphylococcus aureus recombination site for plasmid pS1
gi|849134|gb|U26702.1|SAU26702 [849134]
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- ☐ U21221
Staphylococcus aureus hyaluronate lyase (hysA) gene, complete cds
gi|705405|gb|U21221.1|SAU21221 [705405]
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- ☐ U36379
Staphylococcus aureus S-adenosylmethionine synthetase gene, complete cds
gi|1020316|gb|U36379.1|SAU36379 [1020316]
(View [GenBank report](#), [FASTA report](#), [ASN.1 report](#), [Graphical view](#), or [1 protein link](#))
- ☐ U06451
Staphylococcus aureus proline permease homolog (putP) gene, complete cds
gi|458419|gb|U06451.1|SAU06451 [458419]
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protein link, or 2 nucleotide neighbors)

☐ U35036

Staphylococcus aureus R-plasmid pSBK203 replication initiation protein gene, chloramphenicol acetyltransferase gene, and Pre protein gene, complete cds
gi|1015405|gb|U35036.1|SAU35036 [1015405]

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☐ U20794

Staphylococcus aureus fibrinogen binding protein (fbpA) gene, complete cds
gi|915307|gb|U20794.1|SAU20794 [915307]

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☐ L25426

Staphylococcus aureus penicillin-binding protein 2 (pbp2) gene, complete cds
gi|409240|gb|L25426.1|STAPBP2X [409240]

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☐ M86227

Staphylococcus aureus DNA gyrase B subunit (gyrB) RecF homologue (recF) and DNA gyrase A subunit (gyrA) gene, complete cds
gi|153083|gb|M86227.1|STARECF [153083]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, 1 MEDLINE link, 3 protein links, or 112 nucleotide neighbors)

☐ M63176

Staphylococcus aureus helicase required for T181 replication (pcrA) gene, complete cds
gi|153060|gb|M63176.1|STAPCRA [153060]

(View GenBank report, FASTA report, ASN.1 report, Graphical view, 2 MEDLINE links, or 2 protein links)

☐ L11998

Staphylococcus aureus conjugative transfer gene complex (trs)
gi|310606|gb|L11998.1|STATRSC [310606]

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☐ L05004

Staphylococcus aureus dehydroquinase synthase (aroB) gene, 3' end cds; 3-phosphoshikimate-1-carboxyvinyltransferase (aroA) gene, complete cds; ORF3, complete cds
gi|152954|gb|L05004.1|STAAROA [152954]

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☐ L42764

Staphylococcus aureus (clone pS120+) DNA fragment
gi|852065|gb|L42764.1|STAFRA [852065]

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neighbors)

☐ M32103

Staphylococcus aureus lac repressor (lacR) gene, complete cds and lacA repressor (lacA), partial cds
gi|845685|gb|M32103.1|STALACR [845685]
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☐ U10927

Staphylococcus aureus M type 1 capsular polysaccharide biosynthesis (capA, capB, capC, capD, capE, capF, capG, capH, capI, capJ, capK, capL, capM) genes, complete cds
gi|567035|gb|U10927.1|SAU10927 [567035]
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☐ AH003057

Staphylococcus aureus dihydrolipoamide dehydrogenase E2 subunit gene, partial cds
gi|152993|gb|AH003057.1|SEG_STADLDE [152993]
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☐ M73535

Staphylococcus aureus dihydrolipoamide dehydrogenase E2 subunit gene, 3' end and dihydrolipoamide dehydrogenase E3 subunit gene, 5' end
gi|152992|gb|M73535.1|STADLDE2 [152992]
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☐ M73536

Staphylococcus aureus dihydrolipoamide dehydrogenase E2 subunit gene, partial cds
gi|152991|gb|M73536.1|STADLDE1 [152991]
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☐ U20782

Staphylococcus aureus staphylococcal accessory regulator A (sarA) gene, complete cds
gi|684949|gb|U20782.1|SAU20782 [684949]
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☐ L37598

Staphylococcus auricularis 16S ribosomal RNA (16S rRNA) gene
gi|576604|gb|L37598.1|STARGDC [576604]
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☐ L37597

Staphylococcus aureus 16S ribosomal RNA (16S rRNA) gene
gi|576603|gb|L37597.1|STARGDB [576603]
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neighbors)

☐ L36472

Staphylococcus aureus lysyl-tRNA synthetase gene, complete cds, transfer RNA (tRNA) genes, 5S ribosomal RNA (5S rRNA) gene, 16S ribosomal RNA (16S rRNA) gene, 23S ribosomal RNA (23S rRNA) gene

gi|567883|gb|L36472.1|STA5SRR [567883]

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☐ L25288

Staphylococcus aureus gyrase-like protein alpha and beta subunit (grlA and grlB) genes, complete cds

gi|561878|gb|L25288.1|STAGYRASL [561878]

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☐ L25893

Staphylococcus aureus recA gene, complete cds

gi|463284|gb|L25893.1|STARECAA [463284]

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☐ K02687

S.aureus 5S ribosomal RNA

gi|176018|gb|K02687.1|STARRASA [176018]

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☐ L23109

Staphylococcus aureus recombinase (sin) gene, complete cds

gi|495088|gb|L23109.1|STASINA [495088]

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☐ L07778

Staphylococcus aureus acetyltransferase (vat) gene, complete cds

gi|398084|gb|L07778.1|STAVAT [398084]

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☐ M90056

Staphylococcus aureus plasmid ATP-binding protein (vga) gene, complete cds

gi|153124|gb|M90056.1|STAVGA [153124]

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☐ J02615

S.aureus toxic shock syndrome toxin-1 gene, complete cds

gi|153122|gb|J02615.1|STATSST1 [153122]

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protein link, or 4 nucleotide neighbors)

☐ M18970

S.aureus enterotoxin A (entA) gene, complete cds

gi|153120|gb|M18970.1|STATOXAA [153120]

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☐ K02985

S.aureus (strain RN450) transposon Tn554 insertion site

gi|153118|gb|K02985.1|STATNIS5 [153118]

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☐ M21136

S.aureus tetracycline resistance (tetM) gene, complete cds

gi|153114|gb|M21136.1|STATETM [153114]

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☐ M10501

S.aureus/transposon Tn551 left junction C

gi|153113|gb|M10501.1|STAT551C [153113]

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☐ AH000935

S.aureus/transposon Tn551 left junction B

gi|153112|gb|AH000935.1|SEG_STAT551B [153112]

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☐ M10500

S.aureus/transposon Tn551 right junction B

gi|153111|gb|M10500.1|STAT551B2 [153111]

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☐ M10499

S.aureus/transposon Tn551 left junction B

gi|153110|gb|M10499.1|STAT551B1 [153110]

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☐ AH000934

S.aureus/transposon Tn551 left junction A

gi|153109|gb|AH000934.1|SEG_STAT551A [153109]

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☐ M10498

S.aureus/transposon Tn551 right junction A

gi|153108|gb|M10498.1|STAT551A2 [153108]

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☐ M10497

S.aureus/transposon Tn551 left junction A

gi|153107|gb|M10497.1|STAT551A1 [153107]

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☐ M18264

S.aureus staphylococcal protein A (SPA) gene, complete cds

gi|153105|gb|M18264.1|STASPA [153105]

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☐ J01786

S.aureus spa gene coding for protein A, complete cds

gi|153103|gb|J01786.1|STASPA [153103]

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☐ M33833

S.aureus enterotoxin B (seb) gene, 5' flank

gi|153101|gb|M33833.1|STASEB [153101]

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☐ M32470

S.aureus Sau3AI-restriction-enzyme and Sau3AI-modification-enzyme genes, complete cds

gi|153098|gb|M32470.1|STASAU3AIM [153098]

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☐ M20270

S.aureus neomycin resistance gene, partial cds, and bleomycin resistance gene, complete cds

gi|153095|gb|M20270.1|STARESA [153095]

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☐ J03323

S.aureus plasmid pCW7 REP N protein (rep N) gene, complete cds

gi|153089|gb|J03323.1|STAREPNA [153089]

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☐ M33479

S.aureus ethidium resistance (ebr) and replication protein (repA) genes, complete cds

gi|153087|gb|M33479.1|STAREPEBR [153087]

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☐ M94061

gi|153081|gb|M94061.1|STARECA [153081]

M37888

gi|153078|gb|M37888.1|STACD [153078]

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- ☐ M76714
Staphylococcus aureus peptidoglycan hydrolase gene, complete cds
gi|153066|gb|M76714.1|STAPEPHYD [153066]
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- ☐ M17123
S.aureus nuclease gene, partial cds
gi|153056|gb|M17123.1|STANUC [153056]
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- ☐ M97169
Staphylococcus aureus fluoroquinolone resistance protein (norA) gene, complete cds
gi|153054|gb|M97169.1|STANORAX [153054]
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- ☐ M81346
Staphylococcus aureus (methicillin resistant) leucocidin S-component (lukS) gene, complete cds
gi|475838|gb|M81346.1|STALUKS [475838]
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- ☐ M90693
Staphylococcus aureus glycerol ester hydrolase (lip) gene, complete cds
gi|393265|gb|M90693.1|STAGEHLIP [393265]
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- ☐ M25257
Staphylococcus aureus (clone pUB10) beta-lactamase gene, complete cds
gi|341312|gb|M25257.1|STALACBAF [341312]
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- ☐ M25256
Staphylococcus aureus (clone pII3804) beta-lactamase gene, 5' end

gi|341311|gb|M25256.1|STALACBAE [341311]
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☐ M25255
Staphylococcus aureus (clone pI3796) beta-lactamase gene, 5' end
gi|341310|gb|M25255.1|STALACBAD [341310]
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☐ M25254
Staphylococcus aureus (clone pI1071) beta-lactamase gene, complete cds
gi|341309|gb|M25254.1|STALACBAC [341309]
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☐ M25253
Staphylococcus aureus (clone pS1) beta-lactamase gene, complete cds
gi|341308|gb|M25253.1|STALACBAB [341308]
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☐ M25252
Staphylococcus aureus (clone pPC1) beta-lactamase gene, complete cds
gi|341307|gb|M25252.1|STALACBAA [341307]
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☐ L01055
Staphylococcus aureus gamma-hemolysin components A, B and C (hlgA, hlgB, hlgC) genes, complete cds
gi|295153|gb|L01055.1|STAHLGA [295153]
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☐ M83994
Staphylococcus aureus prolipoprotein signal peptidase (lsp) gene, complete cds
gi|153044|gb|M83994.1|STALSP [153044]
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☐ J03947
S.aureus lincosaminide nucleotidyltransferase (linA) gene, complete cds
gi|153040|gb|J03947.1|STALINA [153040]
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☐ J03479
S.aureus enzyme III-lac (lacF), enzyme II-lac (lacE), and phospho-beta-galactosidase (lacG) genes, complete cds
gi|153036|gb|J03479.1|STALACS [153036]

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☐ M64724

S.aureus tagatose 6-phosphate isomerase gene, complete cds

gi|153032|gb|M64724.1|STALACAA [153032]

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☐ M14372

S.aureus phage L54 attP site

gi|153031|gb|M14372.1|STAL54POP [153031]

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☐ M14371

S.aureus phage L54

gi|153030|gb|M14371.1|STAL54POB [153030]

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☐ M14374

S.aureus phage L54 attL site

gi|153029|gb|M14374.1|STAL54BOP [153029]

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☐ M15215

S.aureus phage L54 attB site

gi|153028|gb|M15215.1|STAL54BOB [153028]

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☐ M36694

B.amyloliquefaciens neutral protease gene, complete cds

gi|153026|gb|M36694.1|STAINVSA [153026]

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☐ M37915

S.aureus gyrase (gyrB and gryA) genes, 3' and 5' ends, respectively

gi|153023|gb|M37915.1|STAGYRAB [153023]

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☐ M12715

S.aureus geh gene encoding lipase (glycerol ester hydrolase)

gi|153019|gb|M12715.1|STAGEH [153019]

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- ☐ J04151
S.aureus fibronectin-binding protein (fnbA) mRNA, complete cds
gi|153017|gb|J04151.1|STAFNBP [153017]
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- ☐ L22566
Staphylococcus aureus enterotoxin A gene
gi|349129|gb|L22566.1|STAENTAB [349129]
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- ☐ L13379
Staphylococcus aureus enterotoxin gene, 3' end
gi|295150|gb|L13379.1|STAENTEROF [295150]
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- ☐ L13378
Staphylococcus aureus enterotoxin gene, 3' end
gi|295148|gb|L13378.1|STAENTEROE [295148]
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- ☐ L13377
Staphylococcus aureus enterotoxin gene, 3' end
gi|295146|gb|L13377.1|STAENTEROD [295146]
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- ☐ L13376
Staphylococcus aureus enterotoxin gene, 3' end
gi|295144|gb|L13376.1|STAENTEROC [295144]
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- ☐ L13375
Staphylococcus aureus enterotoxin gene, 3' end
gi|295142|gb|L13375.1|STAENTEROB [295142]
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- ☐ L13374
Staphylococcus aureus enterotoxin gene, 3' end
gi|295140|gb|L13374.1|STAENTEROA [295140]
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- ☐ M17348

S.aureus exfoliative toxin B (ETB), complete cds

gi|153011|gb|M17348.1|STAETB [153011]

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☐ M17357

S.aureus eta gene encoding epidermolytic toxin A, complete cds

gi|153007|gb|M17357.1|STAETA [153007]

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☐ M17347

S.aureus exfoliative toxin A (ETA), complete cds

gi|153005|gb|M17347.1|STAETA [153005]

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☐ M28364

Staphylococcus aureus enterotoxin C3 gene, complete cds

gi|153003|gb|M28364.1|STAENTTXC [153003]

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☐ M21319

S.aureus enterotoxin type E (entE) gene, complete cds

gi|153001|gb|M21319.1|STAENTE [153001]

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☐ M63917

S.aureus epidermal cell differentiation inhibitor (EDIN) gene, complete cds

gi|152997|gb|M63917.1|STAEDIN [152997]

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☐ M58515

Staphylococcus aureus precursor protein and chloramphenicol acetyltransferase (CAT) genes, complete cds

gi|152980|gb|M58515.1|STACATA [152980]

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☐ L10909

Staphylococcus aureus tnpA gene, tnpB gene, tnpC gene, DS RF gene, complete cds's; cadmium resistance (cadA) gene, complete cds; E1-E2 cadmium efflux adenosine triphosphatase (cadC) gene, complete cds

gi|152973|gb|L10909.1|STACADRES [152973]

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☐ M15067

S.aureus beta-lactamase (blaZ) gene, 5' end

gi|152971|gb|M15067.1|STABLAZA [152971]
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☐ M92376

Staphylococcus aureus beta-lactamase repressor (BlaI) gene, complete cds

gi|152969|gb|M92376.1|STABLAIA [152969]

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☐ M62650

Staphylococcus aureus blaZ gene, 5' end; blaR1 gene, complete cds; blaI gene, complete cds; and binR gene, 5' end

gi|152964|gb|M62650.1|STABLA [152964]

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☐ M32312

S.aureus right arm of secondary Tn554 attachment site

gi|152959|gb|M32312.1|STAATTX [152959]

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☐ M20393

S.aureus bacteriophage phi-11 attachment site (attB)

gi|152958|gb|M20393.1|STAATTB [152958]

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☐ M90536

Staphylococcus aureus alpha-hemolysin gene, 3' end

gi|152952|gb|M90536.1|STAALPHYM [152952]

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☐ M21854

S.aureus agr gene encoding an accessory gene regulator protein, complete cds

gi|152950|gb|M21854.1|STAAGR [152950]

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☐ M36771

S.aureus aminocyclitol-3'-phosphotransferase gene, complete cds

gi|152944|gb|M36771.1|STAAAC [152944]

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☐ L14020

Staphylococcus aureus methicillin-resistance (mecR and mecI) genes, complete cds

gi|295157|gb|L14020.1|STAMECR [295157]

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☐ M81736

Staphylococcus aureus collagen adhesin (cna) gene, complete cds

gi|387879|gb|M81736.1|STACNA [387879]

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☐ U11702

Staphylococcus aureus D4508 enterotoxin H (seh) gene, complete cds

gi|510691|gb|U11702.1|SAU11702 [510691]

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- ☐ L19300
Staphylococcus aureus DNA sequence encoding three ORFs, complete cds; prophage phi-11 sequence homology, 5' flank
gi|310601|gb|L19300.1|STAORFPHI [310601]
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- ☐ L25372
Staphylococcus aureus exfoliative toxin A (eta) gene, complete cds
gi|409062|gb|L25372.1|STASETA [409062]
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- ☐ L22565
Staphylococcus aureus FRI100 enterotoxin A (sea) gene
gi|349128|gb|L22565.1|STAENTAA [349128]
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- ☐ M58516
Staphylococcus aureus precursor protein and chloramphenicol acetyltransferase (CAT) genes, complete cds
gi|152983|gb|M58516.1|STACATB [152983]
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- ☐ U06462
Staphylococcus aureus SA4 FtsZ (ftsZ) gene, complete cds
gi|458427|gb|U06462.1|SAU06462 [458427]
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- ☐ L19298
Staphylococcus aureus phosphatidylinositol-specific phospholipase C (plc) gene, complete cds
gi|425477|gb|L19298.1|STAPIPLC [425477]
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- ☐ M80252

Staphylococcus aureus norA1199 gene (which mediates active efflux of fluoroquinolones), complete cds

gi|295163|gb|M80252.1|STANORA11 [295163]

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☐ L11530

Staphylococcus aureus transfer RNA sequence with two rRNAs

gi|310605|gb|L11530.1|STATRNAA [310605]

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